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HUMAN BEHAVIORAL TEMPERATURE REGULATION: AN EXERCISE APPROACH

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ABSTRACT

Behavior represents our most preferred and effective modality by which body temperature is regulated. However, knowledge concerning the control of this behavior in humans is relatively limited. Therefore, the overall purpose of this thesis was to further our understanding of the control of human thermoregulatory behavior. This was accomplished by firstly establishing self-paced exercise and heat stress as a thermal behavioral model, while secondly the control of this behavior was investigated. In the first part of this thesis, voluntary reductions in exercise intensity have been found to be associated with thermal discomfort and reductions in heat production, which presumably improved heat exchange between the body and the environment over time, and ultimately aided body temperature regulation. Thus, these experimental data associatively indicate that reductions in exercise intensity in the heat are thermoregulatory behaviors, suggesting that self-paced exercise in the heat is a valid model by which to evaluate human thermal behavior. The studies presented in the second part of this thesis systematically evaluated the control of this behavior. It was subsequently demonstrated that skin temperature and the accompanying alterations in thermal perception and the percentage of peak oxygen uptake elicited by a given exercise intensity are all modulators of exercise intensity, and thus thermal behavior, in the heat. Notably, reductions in peak oxygen uptake appear to play a minimal role. Importantly, these studies strengthened the associations observed in the first part of this thesis by specifically establishing a causative relationship between exercise intensity and temperature regulation. Furthermore, the experimental observations also indicated that thermal behavior during self-paced exercise is ultimately initiated by the perception of effort response. In conclusion, the findings presented in this thesis suggest that a voluntary reduction in exercise intensity occurring in the heat is a thermoregulatory behavior, and that this behavior can be directly elicited by changes associated with elevations in skin temperature. During such instances, thermal perception and the percentage of peak oxygen uptake elicited by a given exercise intensity have been uniquely identified as contributors to this behavior. The findings of this thesis improve our understanding of the control of human thermoregulatory behavior.

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LIST OF ABBREVIATIONS

A

ANOVA	Analysis of variance
A-V O ₂	Arteriovenous oxygen content difference
A-V CO ₂	Arteriovenous carbon dioxide content difference

B

bpm	Beats per minute
BSA	Body surface area

C

\dot{C}	Rate of heat exchange via convection
°C	Degrees centigrade
CO ₂	Carbon dioxide
CNS	Central nervous system
\dot{C}_{res}	Rate of heat exchange from respiratory conduction

D

DBP	Diastolic blood pressure
-----	--------------------------

E

\dot{E}	Rate of heat loss via evaporation
EEG	Electroencephalogram
\dot{E}_{max}	Maximal rate of evaporative cooling for heat balance
EMG	Electromyogram
\dot{E}_{req}	Required rate of evaporative cooling for heat balance
\dot{E}_{res}	Rate of heat exchange from respiratory evaporation

G

g	Gram
---	------

H

h	Hour
h _c	Convective heat transfer coefficient
HR	Heart rate
HRpeak	Peak heart rate
%HRpeak	Percentage of peak heart rate
HSI	Heat strain index
H ₂ O	Water

J

J	Joule
---	-------

K

\dot{K}	Rate of heat exchange via conduction
K^+	Potassium
Kg	Kilogram
kJ	Kilojoule
kPa	Kilopascal

L

L	Liter
LCG	Liquid conditioning garment
LF	Linear factor
LR	Lewis relation

M

m	Meter
\dot{M}	Metabolic rate
MAP	Mean arterial pressure
m_b	Body mass
min	Minute
mmHg	Millimeters of mercury
mmol	Millimole
mOsm	Milliosmole

N

Na^+	Sodium
--------	--------

O

O_2	Oxygen
-------	--------

P

P_A	Ambient water vapor pressure
$PO_{RPE\ 16}$	Power output at a rating of perceived exertion of 16
$PO_{70\%}$	Power output at 70% of maximal rate of oxygen uptake
PSI	Physiological strain index
P_{Sk}	Saturated water vapor pressure at the skin

Q

\dot{Q}	Cardiac output
\dot{Q}_{peak}	Peak cardiac output
$\% \dot{Q}_{peak}$	Percentage of peak cardiac output

R

r	Correlation coefficient
\dot{R}	Rate of heat exchange via radiation
RER	Respiratory exchange ratio
RPE	Rating of perceived exertion
rpm	Revolutions per minute

S

s	Second
\dot{S}	Rate of heat storage/loss
SD	Standard deviation
SBP	Systolic blood pressure
SEM	Standard error of the mean

T

T_A	Ambient temperature
T_{aHYP}	Anterior hypothalamic temperature
\bar{T}_b	Mean body temperature
T_C	Core body temperature
thermoTRP	Temperature sensitive transient receptor potential ion channel
TPR	Total peripheral resistance
\bar{T}_{Sk}	Mean skin temperature
TRPM8	Transient receptor potential ion channel Melastatin 8
TRPV1	Transient receptor potential ion channel Vanilloid 1
TRPV3	Transient receptor potential ion channel Vanilloid 3

V

v	Air velocity
$\dot{V}CO_2$	Rate of carbon dioxide elimination
$\dot{V}O_2$	Rate of oxygen uptake
$\dot{V}O_{2max}$	Maximal rate of oxygen uptake
$\dot{V}O_{2peak}$	Peak rate of oxygen uptake
$\% \dot{V}O_{2peak}$	Percentage of the peak rate of oxygen uptake

W

W	Watt
\dot{W}	Rate of heat exchange from the generation of external work

Y

y	Year
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CHAPTER ONE

1.0: Introduction

Energy and matter are constantly exchanged between all living organisms and their environment. This exchange is mediated by a combination of autonomic and behavioral responses (Cabanac 1987, 1996b). Examples of autonomically controlled energy and matter exchange include, amongst others, pulmonary ventilation and evaporative heat loss, while examples of behaviorally mediated responses stretch from such seemingly unrelated actions as defecation to exercise. In accordance, the regulation of a wide variety of physiological processes, and thus whole body homeostasis, is accomplished via a complementary combination of autonomic and behavioral mechanisms (Figure 1.1). Thus, behavior has an important place within physiology (Cabanac 1987, 1996b).

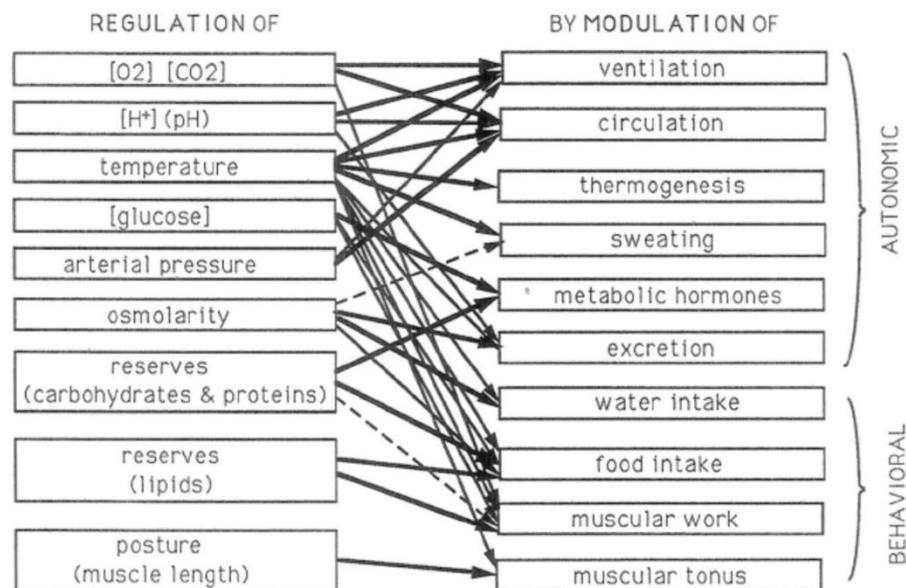


Figure 1.1: The regulation of some physiological variables (on left) as achieved by the modulation of various functions (on right). This is not an exhaustive list. Notably, behavioral responses participate in the regulation of many of the variables (Cabanac 1996b).

The role of behavior in physiology has probably received the most attention within environmental physiology (Cabanac 1996b). The significant role of behavior in temperature regulation is perhaps not surprising as environmental physiology is integrative in nature and deals with, in most cases, the functioning of the entire organism (Burton 1956). The significant role of temperature regulation in behavior is perhaps best highlighted in the observations that stable body temperatures in ectotherms (i.e. ‘cold-blooded’ animals) can be achieved via behavior alone, with little-to-no autonomic capability (Stevenson 1985). In accordance, it is perhaps not unexpected that behavioral responses are often considered the preferred (Werner et al. 2008) and most effective form of temperature regulation (Parsons 2003). The importance of behavior in temperature is usually well appreciated. For instance, the published contributions from the First International Symposium on Temperature Regulation (held in 1968 in New Haven, Connecticut, USA) paid equal attention to behavioral and autonomic thermoregulatory responses (Hardy et al. 1970). Nevertheless, knowledge of its control is far less understood than that of the autonomic responses (e.g. Nagashima 2006; Romanovsky 2007).

A particularly large shortcoming within the knowledge base concerning the control of thermoregulatory behavior is its application in humans. An understanding of the control of human thermoregulatory behavior is particularly important (and interesting) considering our known capabilities to withstand drastically cold (e.g. -50°C , the Alaskan winter) and drastically hot (e.g. $+46^{\circ}\text{C}$, a summer in Death Valley, California) ambient temperatures, which generally lie outside of our autonomic capacity to regulate body temperatures (Romanovsky 2007). The rationale behind this knowledge deficiency is rather uncertain. However, this paucity likely stems from the inherent difficulty associated with identifying functional relationships between thermal stimuli and the initiation of behavior in humans. This may also be complicated by the fact that investigating the control of (homeostatic) behavior straddles the fields of psychology and physiology (Bunge 1989; Cabanac 1996b), and as such, it (thermal behavior) may have simply ‘fallen through the cracks.’ Although these certainly represent significant challenges, given its prominence in temperature regulation, a more complete

understanding of the manner in which behavior contributes to body temperature regulation in humans is warranted.

The role of behavior may be of particular importance during instances of exogenous (i.e. external to the body) heat stress. For instance, throughout its geological history, the Earth has experienced many periods of warming and cooling (Barnosky et al. 2003), and irrespective of the cause, it is reasonably well accepted that the Earth is in a period of substantial warming (CSIRO 2007; Meehl et al. 2007). In accordance, the frequency, intensity and duration of heat waves are projected to increase during the coming decades (Maloney and Forbes 2011; Meehl and Tebaldi 2004; Schar et al. 2004). This poses a significant threat to human health (Honda and Ono 2009), which is most formidable in those populations with an impaired ability to behave; that is, those individuals who are unable to take care of themselves or have a reduced capacity for mobility (e.g. infants, the elderly, mentally ill, etc.) (Basu and Samet 2002; Bouchama 2004; Kilbourne et al. 1982; Semenza et al. 1996). Quite clearly, these findings suggest that the inability to appropriately behave directly influences the risk of heat-related illness and mortality.

Notably however, heat-related illness is not constrained to diseased and at risk populations. Rather, perfectly healthy individuals exercising in the heat place themselves in a situation which, if not treated with caution, could lead to rather detrimental health effects (Armstrong 2003). In accordance, excessive heat production within the body, (e.g. during instances of exercise) is an established risk factor for heat illness (Noakes 2008). Thus, manual laborers, workers, and recreational athletes, alike, are at an elevated risk for heat illness when exposed to high ambient heat loads, which is likely to further increase in the coming decades (Maloney and Forbes 2011). Given behavior's utterly important role in temperature regulation and its apparent role in heat-related illness and death during non-exercise situations, it is likely that behavior may be an important thermoregulatory component during exercise as well. However, evidence for this arrangement is required.

Generally, this thesis aims to identify and evaluate the control of human thermoregulatory behavior during exercise within a healthy population during exposure to exogenous heat stress. It is hoped that the enduring outcome of this work will improve the understanding of the control of human thermoregulatory behavior in general, while also increasing the appreciation of behavior's powerful role within human temperature regulation. Notably, the content of this thesis has been written from the physiologist's perspective. Therefore, the role of behavior in homeostasis has been emphasized, as opposed to the role of temperature regulation within behavior in a broader sense. Furthermore, it is recognized that the psychology of initiating thermoregulatory behavior has been perhaps, unintentionally, simplified or areas of psychological control, unknowingly, overlooked. Nevertheless, this thesis represents a comprehensive and critical review, and investigation into, the control of human thermoregulatory behavior.

The concepts briefly introduced in this chapter will be further explored in the following. Specifically, **Chapter Two** entails a thorough and critical review of the literature. This includes an overview of human temperature regulation during exposure to heat stress, with a particular emphasis on exercise and thermoregulatory behavior. **Chapter Three** explicitly states the research aims, objectives and hypotheses. **Chapter Four** describes the methods that were used in all of the subsequent experimental chapters, while **Chapter Five, Chapter Six, Chapter Seven, Chapter Eight** and **Chapter Nine** contain the experimental chapters designed to meet the objectives of this thesis. These chapters are written as independent manuscripts and as such include a formal introduction, methods, results and discussion. The content of these chapters ranges from describing behavioral responses during exercise in the heat (**Chapter Five** and **Chapter Six**) to understanding the control of this behavior (**Chapter Seven, Chapter Eight** and **Chapter Nine**). Finally, **Chapter Ten** summarizes, discusses, proposes directions for future research, and concludes this thesis.

CHAPTER TWO

2.0: Review of Literature

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This chapter is devoted to a thorough review of the literature. The purpose of this chapter is two-fold. The first objective is to establish guidelines that will be adhered to throughout the remainder of this thesis. This includes defining the core body temperature as the regulated variable, providing a general overview of the regulatory pathways and presenting the factors affecting the manner in which this variable is regulated. Given the nature of this thesis, instances of heat stress, exercise and the role of temperature regulation in behavior were emphasized. The second objective is to critically review the literature concerning the manner in which exercise tolerance is affected by heat stress. This entails an overview of the effects of heat stress on $\dot{V}O_2\text{max}$, exercise time-to-exhaustion and self-paced exercise performance both in the field and in the laboratory. Based upon this literature review, the primary focus of this thesis will be formally stated, while the aims, specific objectives and hypotheses presented.

2.1: Homeothermic Temperature Regulation

The capacity to select a preferred ambient temperature, and thus tissue temperature, extends right through the extant animal kingdom, from flagellated unicellular organisms to mammals and birds (Bligh 1998; Marino 2008). Therefore, provided the organism is capable of locomotion, the capacity to sense thermal disturbances and behaviorally regulate tissue (body) temperatures is not related to any particular evolutionary level. Vertebrates can generally be split into two separate, distinct, groups by the physiological means available in order to regulate body temperatures, i.e. endotherms and ectotherms. This distinction is not associated with the absence or presence of stable body temperatures, but rather it is dependent on the basal rate of metabolism, and thereby the rate of tissue heat production (Bligh 1998).

Mammals and birds have a basal metabolism on the order of 5 - 10 times higher than that of their other vertebrate counterparts (for a given mass and body temperature) (Ivanov 2006). In combination with a larger layer of thermal insulation between itself and the environment (Bligh 1998), mammals and birds therefore have a constant, comparatively high, deep (core) body temperature (Ivanov 2006). In these vertebrates, the source of body heat is internal. Therefore these vertebrates are described as endotherms, which is in contrast to those vertebrates whose source of body heat is derived from the ambient environment (i.e. ectotherms) (Mercer 2001). Although a clear scientific explanation for endothermy is unavailable (Ivanov 2006), it is clear that independence from seeking a suitable environment for heat exchange, and a high core body temperature permitted the rapid development of the central nervous system (CNS) (Ivanov 2006).

Relative to those of ectotherms, the core body temperature of endotherms lies in a narrow range between ~36 and 42°C, with that of a specific species often being maintained more strictly (Ivanov 2006). Thus, endothermy requires the non-behavioral regulation of body temperatures. Hence, most endothermic vertebrates are characterized as homeotherms (Mercer 2001), and are described by their ability to autonomically, involuntarily, regulate body temperatures independent of ambient conditions (Kanosue et al. 2010).

As mammals, humans are endothermic homeotherms, and as such regulate core body temperatures within a narrow range ($37 \pm 1^{\circ}\text{C}$). By using a combination of behavioral and autonomic responses, body temperature regulation allows our species survival despite exposure to drastically extreme ambient temperatures (Figure 2.1). Utilizing a multi-sensor, multi-processor, multi-effector system, the distributed, feedback controlled, thermoregulatory system responds dynamically and proportionally to thermal insults (Werner 2010). Yet, despite this seemingly complex arrangement, in nearly all circumstances core body temperature is regulated in an elegant and synchronous manner.

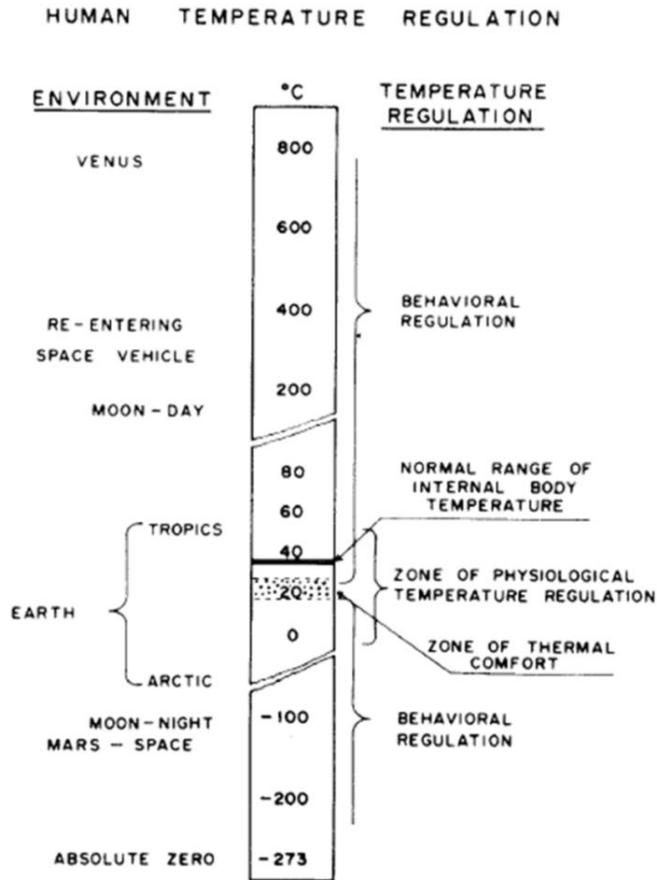


Figure 2.1: Control of body temperature by physiological (autonomic) and behavioral temperature regulation (Hardy 1971). On the left are temperatures of environments that humans could possibly encounter. On the right are thermoregulatory responses in relation to their capabilities and ranges of core body temperature and thermal comfort. The tremendous capability to thermoregulate allows for tolerance of a wide range of thermal conditions.

2.2: Human Temperature Regulation

The aim of human temperature regulation is to maintain a constant core body temperature (T_C) in spite of internal or external thermal disturbances (Kanosue et al. 2010; Mekjavic and Eiken 2006; Romanovsky 2007; Werner 2010). This regulation is achieved via the control of heat loss and heat gain both to and from the body (Cabanac 1997). Heat loss and gain are proportionally modulated by multiple autonomic and behavioral thermo-effectors (Werner 2010). Changes in body temperatures are identified by thermo-sensors spatially, non-uniformly, distributed throughout the body. This information is fed back to thermo-effector controllers. Thereby T_C is regulated via a closed-loop, feedback control system (Werner 2010).

Given the constancy of T_C , and the characteristics of a regulatory system (Cabanac 1997), T_C has typically been considered to be regulated about an adjustable 'set point' (Cabanac 2006a; Hammel 1968). Indeed, in most circumstances body temperature regulation can be sufficiently described in terms of this set point and the regulatory characteristics of biological systems (Cabanac 1997, 2006a). However, evidence indicates that the thermoregulatory system is not operating in such a traditional manner (Kanosue et al. 2010; Kanosue et al. 1997; McAllen et al. 2010; Roberts 1988; Romanovsky 2007; Werner 1980, 2010). This section will provide an overview of the current concepts of human temperature regulation that will be utilized through the remainder of this thesis.

2.2.1: *The Regulated Variable*

Although sometimes problematic (e.g. Jay et al. 2007a; Jay et al. 2007b), for the sake of convenience, the body can be divided into two thermal compartments: the temperature of the body core, i.e. T_C , and that of the body shell, which is typically measured as the temperature of the skin, i.e. mean skin temperature, \bar{T}_{SK} . (Werner 2010). T_C is comprised of the vital organs and the internal mass surrounding the CNS and is monitored at various sites throughout the body (Bligh 1998; Mercer and Jessen 1978a; Romanovsky 2007) - the most important likely being the preoptic area of the hypothalamus (Berner and Heller 1998; Cabanac 2006a; Satinoff 1978). Given its constancy, and that it is generally autonomically defended independent of extremes in ambient temperature, T_C is the

regulated variable (Kanosue et al. 2010; Simon et al. 1986). Thus, the closed-loop, feedback control system defends T_C (Figure 2.2). \bar{T}_{SK} is comprised of fat and skin, and is highly variable (Romanovsky et al. 2002) and strongly dependent upon ambient temperature (Kanosue et al. 2010), therefore it is not regulated. Given such characteristics it has been suggested that \bar{T}_{SK} simply provides thermal sensory information of the thermal environment surrounding the body (Kanosue et al. 2010). However, this is perhaps too simplistic given that \bar{T}_{SK} can vary with thermo-effector driven heat exchange (Nomoto et al. 2004), and therefore temperature regulation.

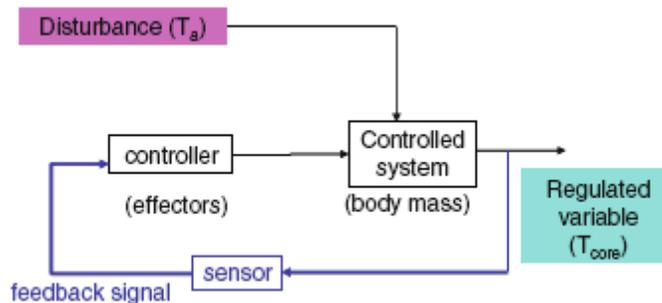


Figure 2.2: The thermoregulatory feedback control loop (Kanosue et al. 2010).

Heat is a function of a temperature difference, the mass of the body, and its specific heat (Anonymous 2009). Therefore, if mass and specific heat remain constant, one might be tempted to conclude that body heat storage is regulated (Cabanac 1997, 2006a). Indeed, heat flow has been suggested to be the primary and decisive regulated variable (Webb 1995). It is out of the scope of this thesis to inclusively review and critique the concepts of temperature and heat regulation. However, it is of interest to provide an explanation for the regulatory concept which will be adhered to throughout this thesis.

Heat is a form of energy and is therefore an extensive variable (Anonymous 2009), while temperature an intensive variable (Anonymous 2009). In regulated physiological systems, all regulated variables are intensive (e.g. temperature, blood pressure,

concentrations, etc.), which is likely due to the fact that biological sensors are sensitive to only intensive variables (Cabanac 1997, 2006a). Additionally, the modulated variables in a regulatory system result in stability of the regulated variable (Cabanac 1997). There is little debate that body heat loss and gain is modulated by autonomic and behavioral responses, and that this results in T_C stability. Therefore heat is the modulated variable, not the regulated variable. Additionally, the fact that body temperatures are adequately maintained during instances where body mass is changed (i.e. growth or amputation) suggests that heat content is not regulated (Cabanac 1975; Hensel 1981). Although an incomplete argument has been provided here, it is suggested the reader refer to the following references: (Cabanac 1975, 1997, 2006a; Hensel 1981; Werner 2010). Notably, Cabanac (2006a) seemingly laid the argument to rest by stating that “[given] that no heat-flow sensor has ever been discovered in the [human] body, the mere fact that ectotherms regulate their body temperature behaviorally, with virtually no heat flow from their body to the environment, is sufficient to rule out the concept...” of heat regulation. Resultantly, temperature, specifically T_C , will be considered the regulated variable throughout the remainder of this thesis.

2.2.2: Core Temperature Regulation

At the systems level, the regulation of T_C is very much demonstrated in the processes described in Figure 2.2. In most circumstances, the human thermoregulatory system does indeed appear to defend a set level of T_C as if it is a unified system operating with a set point (Cabanac 2006a). Alternatively, an analysis of how physiological systems may have evolved (Partridge 1982), together with mounting neurophysiological evidence (Kanosue et al. 1997; McAllen et al. 2010; Roberts 1988; Romanovsky 2007), it is highly unlikely that the human thermoregulatory system utilizes a common neural circuitry in order to defend T_C about an adjustable set point. Rather, the human thermoregulatory system utilizes multiple sensors and processors in order to regulate T_C (Werner 2010).

Although it may appear to operate as being true (Cabanac 1997, 2006a), one should not expect physiological regulatory processes to operate exactly as an engineer would design them (Partridge 1982). For instance, all that is required for a new mechanism to be

conserved is that it improves the animal's chances of survival and reproduction. How elegantly the physiological problem is solved is irrelevant (Partridge 1982). For instance, thermal behavioral responses are supplemented by varying levels of autonomic temperature regulation in modern ectothermic vertebrates, such as reptiles (Seebacher and Franklin 2005). Although these responses operate synchronously to regulate body temperatures, given that these responses evolved at different points on the evolutionary tree, a common neural circuitry is unlikely unless neural coordination provides a further advantage (Partridge 1982). As an example, when autonomic temperature regulation is impaired, homeotherms retain the ability to adequately behaviorally thermoregulate (Almeida et al. 2006b; Carlisle 1969; Satinoff and Rutstein 1970; Schulze et al. 1981), thereby suggesting that the two responses are controlled independently (Satinoff 1978).

Experimental evidence indicates that not only are behavior and autonomous effectors separately controlled, but rather the multiple autonomic effectors are also independently controlled (Kanosue et al. 2010; Kanosue et al. 1997; McAllen et al. 2010; Roberts 1988; Romanovsky 2007). The independent thermo-effector neural pathways involved will be addressed later in this chapter (*see* 2.4: Human Temperature Regulation and Heat Stress). Of particular interest in this section is how afferent thermo-sensory information is integrated and transformed into the appropriate thermo-effector response - whether behavioral or autonomic.

The rostral area of the hypothalamus, referred to as the preoptic area, is recognized as an important neural structure in the homeothermic regulation of T_C . This area consists of the medial and lateral parts of the preoptic nucleus, regions of the nearby septum, and anterior hypothalamus (Boulant 2000). Despite the preoptic areas utter importance, evidence suggests that there is no single neural area acts as *the* center for temperature regulation. Rather, there appears to be a hierarchy of structures extending through the hypothalamus, brain stem, and spinal cord (Boulant 2000), all of which are capable of integrating afferent information and initiating thermoregulatory responses (Gordon and Heath 1986).

Alone, the lower brain stem and spinal structures are capable of sensing temperature changes and initiating the corresponding thermo-effector responses (Boulant 2000). However, when the preoptic area is connected to the lower brain stem, T_C is regulated more precisely (Boulant 2000). The CNS is also more sensitive to changes in temperature with a greater variety of thermo-effector responses being evoked when the connections between the preoptic area and the extra-hypothalamic (brain stem and spinal cord) thermoregulatory areas are intact (Boulant 2000). This is especially true during thermal stressors associated with exercise or changes in environmental temperature (Boulant 2000). Thus, the preoptic area is not the sole integrator of body temperature, but rather it is the most important thermoregulatory center in that it coordinates the activity of other integrating mechanisms at the lower, extra-hypothalamic, neural levels (Berner and Heller 1998; Satinoff 1978). Given that each thermoregulatory center can independently regulate T_C , the proposed rationale behind the recurrent nature of the neural thermoregulatory pathways is that the overall connectivity between the thermoregulatory centers results in the fine control of T_C observed in homeotherms (Gordon and Heath 1986; Kanosue et al. 2010; Kanosue et al. 1997; Romanovsky 2007; Satinoff 1978).

It is in the following manner that the body likely integrates thermal information into the proper thermoregulatory responses. The preoptic area, in addition to the other extra-hypothalamic thermoregulatory centers (Gordon and Heath 1986; Satinoff 1978), receives and integrates thermal afferent signals from thermo-sensors, distributed non-uniformly throughout the body (Mercer and Jessen 1978a, b), including both warm and cold receptors at the skin (Boulant and Hardy 1974). Thermoregulatory responses may be derived from lower, extra-hypothalamic, thermoregulatory centers (Gordon and Heath 1986; Kanosue et al. 2010; Kanosue et al. 1997; Satinoff 1978). However, the preoptic area serves as the final integrator of afferent thermo-sensory information (Berner and Heller 1998; Satinoff 1978). The orderly recruitment of thermo-effector responses is driven by two factors. The first is the aforementioned hierarchy of thermoregulatory centers (Satinoff 1978), while the second involves the multiple independent thermo-

effectors each of which has a different threshold activation temperature (Kanosue et al. 2010).

The threshold temperature at which thermo-effectors are recruited is relative to the location within the CNS hierarchy (Satinoff 1978). For instance, a spinal thermoregulatory center has a thermo-neutral (or null) zone, i.e. a temperature zone in which neither autonomic heat loss (sweating) nor heat gain (shivering) responses are activated (Mekjavic et al. 1991), of 4 - 5°C (Bligh 1973), while a thermoregulatory center located in the preoptic area would have a much narrower thermo-neutral zone (Satinoff 1978). In a human this thermo-neutral zone would be $\sim 37 \pm 0.5^\circ\text{C}$ (Figure 2.3). This hierarchical neural organization explains the necessity for an intact preoptic area for precise T_C regulation, but also explains how temperature can also be adequately regulated independently.

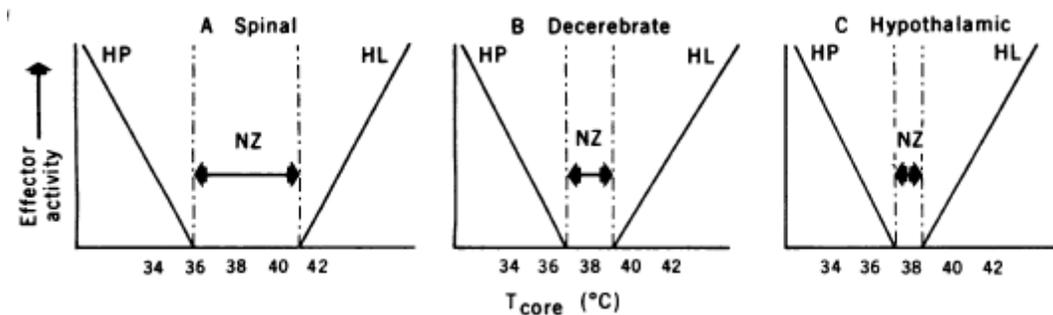


Figure 2.3: The neural hierarchy of temperature regulation according to Satinoff (1978). HP, indicates heat production; HL, indicates heat loss; NZ, is the thermo-neutral zone. Note that the thermo-neutral zone gets smaller as the CNS location moves closer (and into) the hypothalamus.

In addition to the thermoregulatory CNS hierarchy, each of the multiple homeothermic thermo-effectors has an independent neural pathway and different T_C threshold for activation (Kanosue et al. 2010; McAllen et al. 2010). This set-up allows for the orderly recruitment of thermo-effectors. For instance, in humans exposed to heat, cutaneous vasodilation, sweating, and heat avoidance behavior are typically available. Upon heat

exposure, the combination of cutaneous vasodilation and behavior are usually considered the first line of temperature regulation (Bligh 1998; Parsons 2003; Werner et al. 2008). However, if behavior is restricted and cutaneous vasodilation insufficient, sweating will be elicited. This orderly recruitment is likely based upon the thermo-effector thresholds at each hierarchal center. Although there does not appear to be a 'threshold' T_C for the activation of behavioral thermo-effectors (Schlader et al. 2009), it is likely that sweating has a higher T_C threshold than cutaneous vasodilation (Kanosue et al. 2010; Kanosue et al. 1997). Although this strategy may be less optimal for the precise regulation of T_C , the delayed recruitment of sweating is likely an adaptive response because water, a precious resource, is consumed by sweating (Kanosue et al. 2010; Romanovsky 2007). The cold defense responses operate in the same manner with behavior, cutaneous vasoconstriction, and shivering being orderly recruited. Furthermore, this recruitment order conserves energy by delaying shivering (Kanosue et al. 2010; Romanovsky 2007).

Although \bar{T}_{sk} is not a regulated variable, it provides vital feedback concerning the threat of impending thermal insults (Kanosue et al. 2010; Romanovsky 2007; Schlader et al. 2009). Accordingly, the \bar{T}_{sk} inputs are integrated with the T_C inputs and the level of output for the appropriate thermoregulatory responses is established (Boulant 2000). This is perhaps best exemplified by the modifying role \bar{T}_{sk} plays in the control of thermal sweating (*see* 2.4.2: Eccrine Sweating). For instance, \bar{T}_{sk} modifies the T_C threshold at which thermal sweating is initiated, such that when \bar{T}_{sk} is warm sweating is initiated at a lower T_C and vice versa (Shibasaki et al. 2006). It is in this way that \bar{T}_{sk} modifies temperature regulation - by altering the thermo-effector thresholds T_C (Kanosue et al. 2010). Notably, other non-thermal factors (e.g. exercise, dehydration, etc.) can influence these T_C thresholds (Kanosue et al. 2010; Mekjavic and Eiken 2006). Many of these will be individually discussed later in this chapter.

2.2.3: Temperature Sensors

In theory, T_C could be stable and resist transient perturbations and not be regulated (Cabanac 1997). However, homeothermic temperature regulation utilizes thermo-sensors

spatially, non-uniformly, distributed throughout the body that provide feedback of the thermal status of the body (both T_C and \bar{T}_{Sk}) (Werner 2010). The afferent information provided by these thermo-sensors is integrated at the various, aforementioned, hierarchal thermoregulatory centers and the appropriate thermo-effector elicited. Therefore T_C is maintained via a regulated system (Cabanac 1997, 2006a). Thermo-sensors are directly responsive to changes in their temperature (Bligh 1998), and can be described by three well-established features (Figure 2.4).

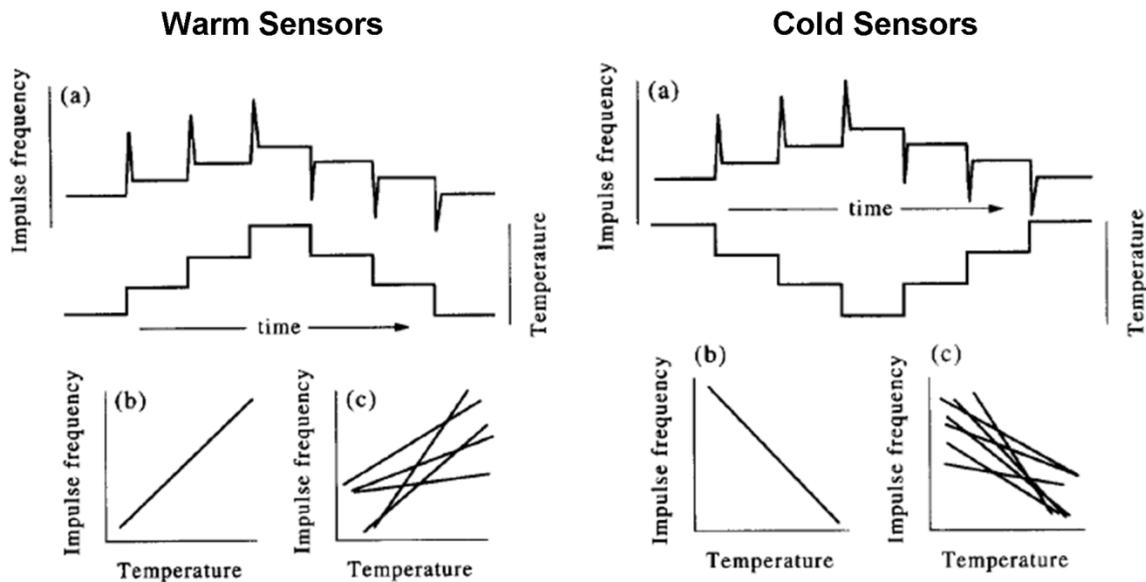


Figure 2.4: Warm (on left) and cold (on right) sensor responsiveness to (a) stepwise changes in temperature. (b) An idealized plot of sustained impulse frequency at steady-state temperatures. (c) An indication of the variability between individual warm sensors (Bligh 1998).

The first feature is that over a physiologically relevant range of temperatures some sensors increase their neural firing rate as temperature increases, i.e. warm sensors (Figure 2.4, on left), while others increase their neural firing rate as temperature decreases, i.e. cold sensors (Figure 2.4, on right). Thus, thermo-sensors are specifically

classified as either warm or cold sensors (Bligh 1998; Dostrovsky and Hellon 1978; Hensel 1981).

The second feature is that thermo-sensors respond to a change in temperature with a brief burst of activity. Then if the temperature increment is sustained the neural firing rate subsides to a steady level which is higher/lower than that before the incremental change in temperature. This level of activity is sustained for as long as the temperature remains constant (Figure 2.4a) (Bligh 1998; Dostrovsky and Hellon 1978).

The final feature is that when the steady-state firing rate at given temperatures is plotted against those temperatures, there is more or less a linear relationship (Figure 2.4b). However, the slopes of these plots vary greatly between thermo-sensors (Figure 2.4c). The functional significance of this phenomenon remains unknown (Bligh 1998; Dostrovsky and Hellon 1978).

For the sake of convenience thermo-sensing can be separated into central and peripherally derived thermo-sensors. It is important to point out that although these areas have the highest density of thermo-sensitivity, perhaps more than 50% of thermo-sensors lie outside these specified areas, and these areas are also important in the regulation of T_C (Mercer and Jessen 1978a, b). The characteristics of central and peripheral thermo-sensation are addressed in the following.

2.2.3.1: Central Thermo-sensors

Central thermo-sensors are contained within the CNS in such locations as the spinal cord, brain stem, and preoptic area (Romanovsky 2007). As mentioned previously, these locations all have the capacity to not only sense temperature, but to elicit the appropriate thermoregulatory responses (Satinoff 1978).

Warm and cold thermo-sensors are heterogeneously distributed throughout the body. Warm sensors are in a higher abundance centrally, than are cold sensors (Boulant and Dean 1986; Hardy et al. 1964). This abundance appears optimal for a couple of reasons.

Firstly, T_C is regulated very near the upper lethal limit, while relatively far from the lower lethal limit. Thus, T_C hyperthermia is more dangerous than hypothermia (Romanovsky 2007). Accordingly, compared to cooler conditions, temperature regulation is more sensitive to increases in temperature (Almeida et al. 2006a; Schlader et al. 2009; Stitt et al. 1971). Secondly, humans are endothermic homeotherms, and therefore sensors for limiting heat gain must be located inside the body, as opposed to located peripherally (Romanovsky 2007).

Given their relatively small population (Boulant and Dean 1986; Hardy et al. 1964), cold sensors play a more minor role in central thermo-sensation. Cold sensor activity appears to be primarily due to synaptic inhibition from nearby warm sensors rather than inherent activity (Boulant and Dean 1986), and accordingly, both cold- and heat-defense responses are predominately triggered by changes in the activity of warm sensors. For instance, increased activity of preoptic warm sensors elicits heat-defense responses, while decreased activity elicits cold-defense responses (Chen et al. 1998; Zhang et al. 1995a).

It is obvious that central thermo-sensation may develop without peripheral thermo-sensation. However, afferent peripheral activation is often followed by central thermo-sensation (Nomoto et al. 2004). Therefore, central thermo-sensation would be expected to play the following roles: 1.) Setting the basal tone of thermo-effector responses; 2.) Enhancing thermo-effector responses in situations of extreme thermal environments where the responses of the ‘lower’ thermal integration sites have proven inadequate to prevent changes in T_C ; and 3.) In responding to thermal challenges involving changes in temperature within the body, e.g. exercise, the intake of cold fluids, or hemorrhage (Morrison et al. 2008).

2.2.3.2: Peripheral Thermo-sensors

Peripheral thermo-sensors are primarily located in the skin and in the oral and urogenital mucosa, and are considered to be part of the peripheral nervous system (Romanovsky 2007). Cold sensors appear to be distributed more densely peripherally than warm sensors (Hensel 1981), which is perhaps not surprising given the predominance of warm

sensors centrally (Romanovsky 2007). Cold sensors are located in or immediately beneath the epidermis, and their signals are conveyed via thin myelinated A δ fibers (Hensel 1981; Romanovsky 2007). The less common warm sensors are located slightly deeper in the dermis and their signals are conveyed via unmyelinated C fibers (Hensel 1981; Romanovsky 2007). The dynamic component of the activation of thermo-sensors (i.e. the brief burst of activity when temperature changes, Figure 2.4a) is very important in peripheral thermo-sensation given that peripheral thermo-sensors are more likely to encounter drastic temperature changes than those located centrally. Such a drastic response to transient changes in temperature, and the capability to quickly stabilize activity levels when temperature remains constant (Figure 2.4a), enables the body to rapidly react to thermal challenges (Romanovsky 2007).

Knowledge of the neuronal basis of peripheral thermo-sensation has been improved with the relatively recent discovery of temperature sensitive transient receptor potential ion channels (thermoTRP). ThermoTRP channels are likely involved in the molecular ‘first step’ of peripheral thermo-sensation (Green 2004). The activation of thermoTRP channels results in an inward non-selective cationic current which, consequently, increases the resting membrane potential (Romanovsky 2007). Given this ionic mechanism, it is likely these channels play more of a role in peripheral thermo-sensation (Morrison et al. 2008; Okazawa et al. 2002), rather than central (i.e. preoptic) thermo-sensation (Zhao and Boulant 2005).

Of the ~30 mammalian TRP channels, divided across six subfamilies (Romanovsky 2007), approximately six thermoTRP channels have been found to play a major role in thermo-sensation and temperature regulation (Dhaka et al. 2006; Montell and Caterina 2007; Patapoutian et al. 2003; Story 2006). Each of these thermoTRP channels is activated by a relatively small range of temperatures with differing sensitivities. However, the range they collectively cover is very wide, from noxious (painful) heat ($\geq 43^{\circ}\text{C}$) to noxious cold ($\leq 12^{\circ}\text{C}$) (Dhaka et al. 2006; Montell and Caterina 2007; Patapoutian et al. 2003; Romanovsky 2007; Story 2006) (Table 2.1). Notably, each of the thermoTRP channels can be activated non-thermally. The specific non-thermal

activation of TRPV1 and TRPM8 will be discussed in detail later in this thesis (*see Chapter Eight*).

Table 2.1: Names, activation temperatures, and non-thermal agonists of thermoTRP channels.

ThermoTRP Channel	Activation Temperature	Non-thermal Agonists
TRPV2	$\geq 52^{\circ}\text{C}$	growth factors
TRPV1	$\geq 42^{\circ}\text{C}$	capsaicin, lipoxygenase, acidic pH, resiniferatoxin, NADA, anandamide, ethanol, camphor
TRPV3	$\geq 33^{\circ}\text{C}$	camphor, 2-APB
TRPV4	$\sim 27\text{-}42^{\circ}\text{C}$	hypotonic, phorbol esters
TRPM8	$\leq 25^{\circ}\text{C}$	menthol, icilin, eucalyptol
TRPA1	$\leq 17^{\circ}\text{C}$	cinnamaldehyde, mustard oil, allicin, icilin

Modified from (Patapoutian, Peier et al. 2003; Dhaka, Viswanath et al. 2006).

Although thermoTRP channels undoubtedly play a major role in temperature regulation, it is perhaps too simplistic to assume thermoTRP channels to be the sole molecular means of peripheral thermo-sensation. It is highly likely that thermo-sensation involves the interaction of specialized receptors that work together with ionic channels and additional proteins (Dhaka et al. 2006; Patapoutian et al. 2003) which allows the detection of small changes in temperature (Patapoutian et al. 2003). ThermoTRP channels are therefore not the sole molecular mediators of peripheral thermo-sensation, but rather, an important factor. However, a complete overview of molecular thermo-sensation is out of the scope of this chapter.

2.2.4: Afferent Thermoregulatory Pathways

The homeothermic thermoregulatory system is primarily described in terms of a feedback loop (Werner 1980, 2010). Therefore, peripheral thermo-sensation would be of little use to the body unless the thermal information was fed back through the peripheral nervous

system to an integration site (e.g. the spinal cord, preoptic area, etc.), capable of eliciting the appropriate thermo-effector. These afferent neuronal pathways can be broken down into two distinct pathways (Morrison et al. 2008), those that are involved in autonomic control and those involved in conscious thermal sensation, (dis-)comfort, and thus behavior. These two pathways share the same peripheral thermo-sensory neurons passing through the peripheral nervous system, but diverge at the lamina I in the spinal cord (Craig 2002; Romanovsky 2007). Thus, the nuclei of the lamina I serve as the origin of the thermal afferent neuronal pathways (Nomoto et al. 2004). These pathways are described in Figure 2.5 and as follows.

2.2.4.1: Autonomic Control Pathway

The afferent neuronal pathway involved in autonomic thermoregulatory control is referred to as the spino-parabrachial-preoptic pathway (Morrison et al. 2008). This pathway contains identified relays leading from the spinal cord to the parabrachial nucleus within the pons of the brain stem terminating in the preoptic area of the hypothalamus (Nakamura and Morrison 2008a, b) (Figure 2.5). Notably, each of these relay locations has been identified as being capable of thermal integration, therefore a given afferent thermo-sensory signal could elicit the appropriate thermo-effector response without the signal reaching the preoptic area (Gordon and Heath 1986; Satinoff 1978).

2.2.4.2: Thermal Sensory Pathway

The afferent neuronal pathway involved in conscious thermal perception is referred to as the spino-thalamo-cortical pathway (Craig 2002; Morrison et al. 2008). In contrast to the spino-parabrachial-preoptic pathway, this afferent neuronal pathway leads from the spinal cord, via Lamina I neurons (Craig et al. 2001; Han et al. 1998), to the posterior part of the ventromedial nucleus in the thalamus (Blomqvist et al. 2000; Craig et al. 1994), bypassing relays in the brain stem and hypothalamus (Craig 2002). This thermal sensory afferent pathway terminates in the insular cortex (Figure 2.5) which has been implicated as the primary brain region involved in conscious thermal sensation (Craig et al. 2000; Guest et al. 2007; Hua le et al. 2005; Iannetti et al. 2003; Rolls et al. 2008). Given that appropriate thermal behavioral responses in rats have been found to be localized in the

prefrontal cortex (Shibata et al. 1983a, 1984; Shibata et al. 1983b; Shibata et al. 1985), a cortical area comparable to the insular cortex in humans (Nomoto et al. 2004), the spino-thalamo-cortical pathway is likely directly involved in the initiation of behavioral thermo-effectors (Morrison et al. 2008; Nomoto et al. 2004).

The control of human thermoregulatory behavior will be thoroughly discussed later in this chapter (*see* 2.4.4: Thermoregulatory Behavior). However, the afferent neuronal pathway(s) likely involved in the initiation of thermoregulatory behavior will be addressed presently. The decision to behaviorally thermoregulate is dictated by the hedonics (or affect) of a given thermal sensation. Thus, behavior is driven not by whether a given stimulus is perceived as warm or cool, but rather whether the stimulus is deemed (un-)pleasant (Cabanac 1971, 1987, 2005) or (un-)comfortable (Chatonnet and Cabanac 1965). Accordingly, the orbitofrontal (Guest et al. 2007; Rolls et al. 2008) and the pregenual cingulate (Grabenhorst et al. 2008; Guest et al. 2007; Rolls et al. 2008) cortical areas have been implicated in determining the (dis-)comfort of a given thermal stimulus (Figure 2.5). Likewise, decision-making based upon a given thermal stimulus, i.e. whether one would voluntarily select a thermal stimulus in the future, is primarily derived from the medial prefrontal area 10 cortical region (Grabenhorst et al. 2008), which receives projections from the pregenual cingulated cortex (Carmichael and Price 1996). Additionally, the anterior cingulate cortex also appears to be involved when the decision made initiates an action (Grabenhorst et al. 2008). Thus, it is in these regions that a thermal stimulus is sensed, deemed (un-)comfortable and a decision whether or not to behave is made (Figure 2.5).

Having roughly described this circuitry it is important to note that no one cortical area makes a decision on its own. Each of the areas involved in decision-making are connected by reciprocal forward and backward pathways (Grabenhorst et al. 2008). For instance, although the medial prefrontal area 10 appears to be a terminal cortical location in decision-making, the medial prefrontal area 10 has direct, apparently backward, connections to the insular and orbitofrontal cortices (Petrides and Pandya 2007). Additionally, it is acknowledged that the described afferent pathway involved in

behavioral temperature regulation is perhaps incomplete. For example, the amygdala has been found to be activated during instances of unpleasant cold stress (Kanosue et al. 2002), yet this neural location lies outside of the spino-thalamo-cortical pathway.

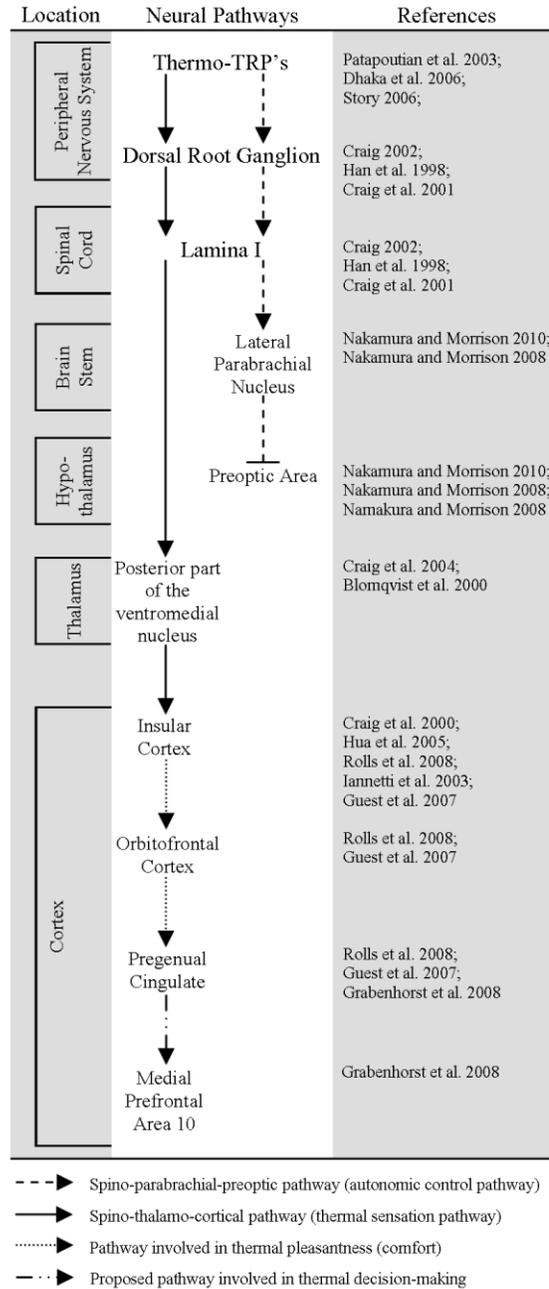


Figure 2.5: Afferent neuronal pathways involved in autonomic control and those involved in conscious thermal sensation, (dis-)comfort, and behavior. These pathways involve the same neural structures through the peripheral nervous system and lamina I neurons, after which the pathways diverge. The afferent neuronal pathway for autonomic control is the spino-parabrachial-preoptic pathway, while the neuronal pathway for conscious thermal sensation is the spino-thalamo-cortical pathway. The hedonic (affective) value of a given thermal sensation and making a decision based on the pleasantness of that stimulus is dictated by activity in other connected cortical locations.

The fundamental concepts of central and peripheral thermo-sensation, the afferent neuronal relays, the hierarchal integration of the afferent signals, and that T_C represents the regulated variable will be adhered to throughout the remainder of this thesis. The following sections address the biophysics of heat exchange, the human body, and its thermo-effector responses. Given the nature of this thesis, an emphasis will be placed on heat defense.

2.3: Heat Exchange and the Human Body

2.3.1: Thermodynamics, Heat, and Temperature

Repeated observations of events in the physical world reveal that two fundamental laws always hold true (Brooks et al. 2005). This first law (of thermodynamics) states that the kinetic and potential energy of the molecules and atoms in a system cannot be created nor destroyed, only transferred from one system to another in the form of heat (Anonymous 2009). The second law (of thermodynamics) gives an indication of the direction of heat transfer; thus introducing the concept of temperature (Anonymous 2009). Temperature is the average kinetic energy in a system, and heat energy flows from a system of high temperature to a system of lower temperature, i.e. down a thermal gradient (Anonymous 2009). Therefore, a system is said to be in thermal equilibrium (heat balance) when there is no change in temperature over time (Anonymous 2009). The human body is a system. Thus, the laws of thermodynamics directly impact the manner in which heat is lost and/or gained by the body.

2.3.2: Heat Balance

The goal of homeothermic temperature regulation is to constantly maintain T_C independent of the ambient environment. Therefore, although heat is exchanged dynamically throughout the life of an individual, heat balance is achieved nearly constantly. Humans have developed distinct autonomic and behavioral capacities that enable us to maintain heat balance despite both internal and external thermal insults. Thus, we are, quite simply, able to balance body heat gain with body heat loss. This concept is portrayed in the heat balance equation (Equation 2.1) (Mercer 2001).

Equation 2.1: The heat balance equation

$$\dot{S} = \dot{M} \pm \dot{W} \pm \dot{E} \pm \dot{R} \pm \dot{C} \pm \dot{K} \pm \dot{C}_{res} \pm \dot{E}_{res}$$

Where: \dot{S} is the rate of heat storage (in W/m^2); \dot{M} is metabolic rate (in W/m^2); \dot{W} is the rate of heat transfer from the generation of external work (in W/m^2); \dot{E} is the rate of heat

exchange via evaporation (in W/m^2); \dot{R} is the rate of heat exchange via radiation (W/m^2), \dot{C} is the rate of heat exchange via convection (W/m^2); \dot{K} is the rate of heat exchange via conduction (W/m^2); \dot{C}_{res} is the rate of heat exchange from respiratory conduction (W/m^2); \dot{E}_{res} is the rate of heat exchange from respiratory evaporation (W/m^2).

As can be seen from the heat balance equation (Equation 1), \dot{S} is purely a function of body heat loss (-) and body heat gain (+). When \dot{S} is equal to zero, i.e. heat loss equals heat gain, the body is said to be in heat balance. Body heat gain ($+\dot{S}$) occurs in one of two ways: 1.) The rate of endogenous (metabolic) heat production (i.e. $\dot{M} \pm \dot{W}$) is greater than rate of heat dissipation to the environment; or 2.) The temperature of the fluid (e.g. air, water, etc.) or surface in contact with the body is greater than the capacity of the body's heat dissipating mechanisms. Heat loss ($-\dot{S}$) occurs when the rate of metabolic heat production is lower than the rate of heat loss to the environment. \dot{S} is directly dependent on the modes of heat exchange comprising the heat balance equation (Equation 1). Changes in \dot{S} , to varying degrees, are reflected in changes in body temperatures (both T_C and \bar{T}_{sk}) (Mercer 2001). Thus, temperature regulation modulates heat loss and heat gain, thereby maintaining heat balance and T_C , the regulated variable (Cabanac 1997).

2.3.3: Heat Exchange Modalities and Parameters

The rate of heat exchange, both to and from the body, occurs via four distinct modalities: conduction, convection, radiation and evaporation. Conduction, convection and radiation are driven by a thermal gradient and hence considered modes of sensible heat exchange (Kerslake 1972). By contrast, temperature differences are not directly involved in evaporative heat loss and accordingly, evaporation is considered a mode of insensible heat exchange (Kerslake 1972). Heat exchange is driven by the ambient environment and the characteristics of the individual in that environment. Thus, heat exchange between the body and the environment is driven by the following heat exchange parameters: ambient temperature, radiant temperature, air velocity, humidity, body surface area, clothing, and metabolic heat production (Parsons 2003). These parameters and heat

exchange modalities are altered in order to regulate T_C , thereby maintaining a state of thermal balance throughout life. An overview of the heat exchange modalities and parameters during exercise is presented in Figure 2.6. In the following, each of the heat exchange modalities and parameters is defined with direct regards for autonomic human temperature regulation. Notably, although not implicitly stated in the following, humans are behaviorally capable of modulating heat gain/loss via manipulating many (if not all) of the following heat exchange modalities and parameters.

2.3.3.1: Sensible Heat Exchange

Conduction (\dot{K}):

Conduction is the rate of transfer of heat through direct contact between a system and a solid material, or *non-moving* gas or fluid down a thermal gradient (Mercer 2001). Thus, conduction is dependent upon the thermal gradient and the thermal resistance between the two systems (Kerslake 1972). Unless the skin is in direct contact with an object, conduction is usually considered negligible (Butera 1998). This is predominantly because the transfer of heat within the body occurs between *moving* gases or fluid.

Convection (\dot{C}):

Convection is the rate of conduction of heat from a system to or from a *moving* gas or fluid. There are two types of convection: 1.) Natural convection; and 2.) Forced convection. Natural convection occurs down a thermal gradient with the movement of the gas or fluid being driven by changes in the density of the fluid as a result of heat exchange (Kerslake 1972). With regards to the human body, this occurs constantly. When ambient temperature is cooler than \bar{T}_{Sk} , the air surrounding the body is heated, reducing the density of the air and causing it to rise. The opposite is true when ambient temperature is warmer than \bar{T}_{Sk} . Thus, the temperature gradient between this moving gas and the \bar{T}_{Sk} dictates heat loss/gain. During forced convection the movement of the gas or fluid is not driven by changes in density, and occurs via forced movement of the gas or fluid surrounding the system (Kerslake 1972). Examples of forced convection between \bar{T}

T_{sk} and ambient temperature include the effect of wind or movement on the system (Mercer 2001).

Forced convection is the primary means of heat transfer within the human body. When \bar{T}_{sk} is cooler than that of T_C , as is usually the case, heat from the body core is transferred to the skin for dissipation to the ambient environment via convection (Mercer 2001). This heat exchange is generally driven by the T_C -to- \bar{T}_{sk} gradient (Mercer 2001). However, the magnitude of heat exchange occurs via the circulatory system and (re-)distribution of blood either towards or away from the skin. Thus, when ambient temperature is cooler than \bar{T}_{sk} and heat loss is greater than heat gain, skin blood flow is reduced via cutaneous vasoconstriction thereby reducing convective heat loss. The opposite is true during instances where heat gain is greater than heat loss. Skin blood flow is increased in order to facilitate heat loss to the environment. Notably, convection from respiration (C_{res}) also contributes to the overall heat loss/gain status of the body. The physiological control of skin blood flow will be discussed in more detail later in this chapter (see 2.4.1: Cutaneous Vasodilation and Cardiovascular Adjustments).

Radiation (\dot{R}):

Radiation is the rate of transfer of heat energy between a system and the environment via electromagnetic waves (Kerslake 1972). Intervening air is not involved (Parsons 2003). All matter not at absolute zero (0 Kelvin) absorbs and emits thermal radiation (Mercer 2001). With regards for heat loss both to and from the body, radiation is dependent on the thermal gradient (in Kelvin) between \bar{T}_{sk} and ambient temperature. For most indoor environments radiation is usually driven by ambient temperature. However, when in an outdoor environment, radiant sources differ with exposure to the sun and other surrounding objects (Kenney 1998).

2.3.3.2: Insensible Heat Exchange

Evaporation (\dot{E}):

Evaporation is the rate of heat loss via evaporation. Evaporation only results in heat loss, while condensation, the opposite of evaporation, results in heat gain, but occurs rarely with regard to human temperature regulation. As mentioned previously, the rate of evaporation is not driven by a thermal gradient. Rather, it is dependent on the absolute humidity gradient between the skin and the ambient environment. When the absolute humidity at the skin is greater than that of the ambient environment, heat is lost. The amount of heat lost is dependent upon the latent heat of vaporization of water (at a given temperature) and the amount of water available for evaporation (Mercer 2001). The latent heat of vaporization of sweat is ~ 680 W/h/L (Kenney 1998), but this not a constant value.

Human thermoregulatory processes regulate the amount of water on the skin via the control of sweat secretion. It is in this way that heat loss via evaporation is controlled. It is also important to note that although its contribution is relatively small, evaporation via respiration (\dot{E}_{res}) also contributes to the overall heat loss from the body. Sweating, and thus evaporative heat loss, become particularly important when the temperature gradient between \bar{T}_{sk} and the ambient environment is reduced and radiative and convective heat loss are minimized. Under these conditions the body is heavily reliant on evaporation to dissipate heat (Taylor 2006). The physiological control of sweating will be discussed in more detail later in this chapter (*see* 2.4.2: Eccrine Sweating).

2.3.3.3: Heat Exchange Parameters

The amount of heat lost or gained by the body is dependent upon the ambient environment to which the body is exposed. These include: ambient temperature, the radiant temperature, air velocity, humidity, body surface area, clothing, and metabolic heat production (Parsons 2003). These parameters are discussed below.

Ambient Temperature:

Ambient temperature can be defined as the mean temperature of the air surrounding the human body that determines heat flow between the human body and the air (Parsons 2003). Naturally, ambient temperature varies throughout the ambient environment, and may not be necessarily indicative of the capacity for heat exchange - as this is affected by clothing, posture, etc.

Radiant Temperature:

Radiative heat exchange occurs between all bodies not at absolute zero. As radiative heat transfer occurs between the body and all surrounding objects, any point in space represents a unique radiation environment. Radiant temperature is particularly important where relatively large radiant sources are present, i.e. a furnace, the sun, a hot/cold wall, etc. (Parsons 2003).

Air Velocity:

Air velocity directly influences the rate of convective and evaporative heat exchange. Although air velocity is multi-directional, it is meant to mean the average air velocity surrounding the body at any given time. In combination with ambient temperature and humidity, air velocity affects the rate at which air or water vapor is removed from the body (Parsons 2003).

Humidity:

Humidity is the partial pressure of water vapor in the air. Humidity is commonly expressed in two ways: relative humidity and absolute humidity. Relative humidity is the ratio of the actual partial pressure of water vapor in the air versus the saturated water vapor pressure, and is often expressed as a percentage (Kerslake 1972). Absolute humidity is the mass concentration, or density, of water vapor (Kerslake 1972). The rate of evaporative heat loss is driven by the absolute humidity gradient between the skin and the air surrounding the body (Parsons 2003). Notably, the absolute humidity of the air is roughly exponentially dependent on air temperature (Cheung 2010a).

Body Surface Area:

Body surface area represents the surface area in which heat exchange between the body and the ambient environment can occur. It is traditionally estimated from height and weight (Dubois and Dubois 1916). As body surface area typically differs between individual, heat exchange is usually quantified relative to body surface area (Kerslake 1972; Parsons 2003).

Clothing:

The heat exchange responses between the body, clothing and the surrounding air is complex, dynamic and not well understood as it is difficult to quantify (Parsons 2003). Clothing represents a thermal barrier mostly inhibiting sensible and insensible heat loss from the body to the environment (Parsons 2003).

Metabolic Heat Production:

According to the first law of thermodynamics, the energy of a system remains constant. However, this energy may be changed from one form of energy to another. The metabolism of the human body converts chemical potential energy (carbohydrates, lipids, and proteins) into cellular work and heat which maintains the biological processes of the body. As the metabolic rate increases, such as during work or exercise, the rate of endogenous heat production increases. This increase in heat production is due to only ~20% of the converted chemical potential energy being useful in the execution of external work, while the other ~80% appearing as heat energy (Parsons 2003; Taylor 2006). Thus, metabolic heat production is defined as the difference between the total energy produced and the total external work performed by the body (i.e. $\dot{M} \pm \dot{W}$) (Parsons 2003).

As with most thermo-effectors, metabolic heat production is dictated by both autonomic and behavioral control. The autonomic control is depicted in shivering. When heat loss is greater than heat gain and thus T_C falls despite circulatory adjustments, shivering is elicited. During shivering the muscles contract involuntarily yet produce no physical work (Parsons 2003). Thus, heat gain is increased via an increase in metabolism helping

to prevent a further reduction in T_c . Metabolic heat production can also be controlled behaviorally, which will be discussed in further detail later in the chapter (see 2.5.5: Behavioral Control of Exercise Intensity).

2.3.4: Thermal Compensability

Of vast importance to individuals exposed to extreme environmental conditions is the compensability of the thermal environment. Thermal compensability defines the interaction of the body and its heat dissipating mechanisms with the surrounding environment. If the autonomic ability of the body enables the achievement of heat balance then the environment is termed compensable. However, if the ability of the body to lose heat to the environment is greater than the rate of metabolic heat production the environment is uncompensably hot (Cheung et al. 2000). This relationship can be quantified as the ratio of the required rate of evaporative cooling for heat balance (\dot{E}_{req}) and the maximal rate of evaporative cooling for heat balance (\dot{E}_{max}), which is termed the heat strain index (HSI) (Belding and Hatch 1955). Thus, the HSI serves as an index to estimate the thermal compensability of a given environment (Cheung et al. 2000). An $HSI > 1.0$ indicates an uncompensable thermal environment in which heat balance cannot be attained, while an $HSI < 1.0$ indicates a compensable thermal environment (Cheung et al. 2000).

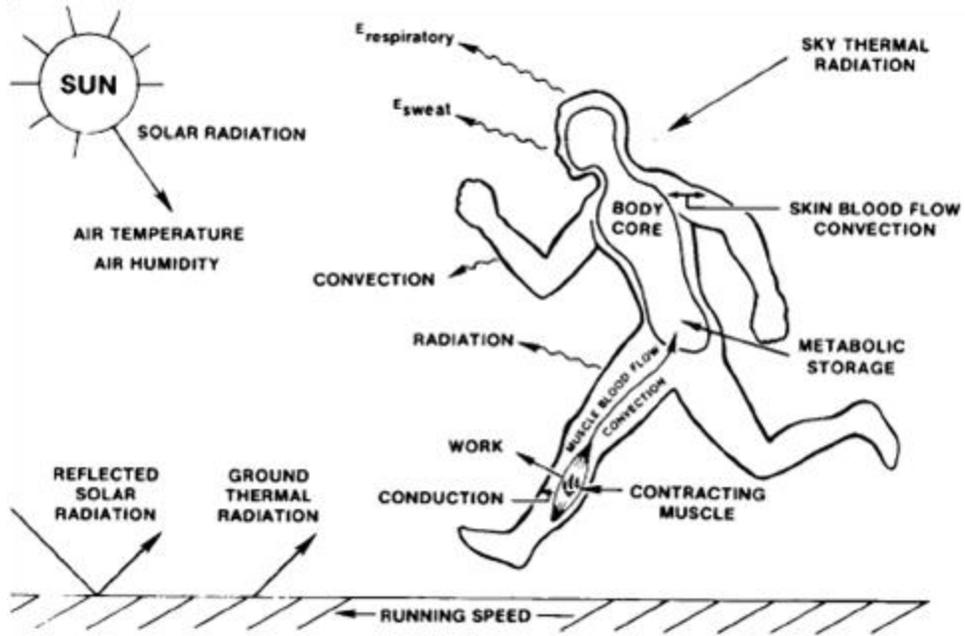


Figure 2.6: Schematic diagram showing heat production within working skeletal muscle, its transport to the body core and to the skin, and its subsequent exchange with the environment (Gisolfi and Wenger 1984).

2.4: Human Temperature Regulation and Heat Stress

Homeotherms, including humans, utilize a combination of behavioral and autonomic responses in order to regulate T_C . Behavior involves voluntarily adjusting the external or internal thermal environment while the autonomic thermoregulatory responses redistribute cardiac output and/or elicit such responses as sweating or shivering. This section will outline the roles and the control of the autonomic and behavioral thermoregulatory responses responsible for temperature regulation during instances of heat stress. Given the nature of this thesis the control of regional blood flow, sweating and heat acclimatization/acclimation are merely introduced, while an emphasis has been placed on behavioral temperature regulation.

2.4.1: Cutaneous Vasodilation and Cardiovascular Adjustments

Cutaneous vasodilation (i.e. increased skin blood flow) and sweating (*see* 2.4.2: Eccrine Sweating) are essential for heat dissipation during instances of heat stress and/or exercise (Charkoudian 2003). The stimulus for cutaneous vasodilation is derived from various locations within the neural thermoregulatory hierarchy, and as such cutaneous vasodilation can be elicited by both reflex (i.e. T_C) and local (skin) temperature changes. Although the outcomes, an increased skin blood flow, are the same, the mechanisms responsible for reflex and local control vary. Further, the endogenous thermal stress elicited by exercise provides a unique challenge to the cutaneous vasodilator response.

Resting skin blood flow in a moderate thermal environment is ~ 2.3 ml/100 ml/min, which results in convective heat loss of $\sim 335 - 378$ kJ/h, approximately counteracting the level of resting metabolic heat production (Johnson et al. 1986). During instances of heat stress cutaneous vasodilation, and the several fold increase in skin blood flow, controls convective heat loss transferring heat from the body core to the periphery. Together with the evaporation of sweat from the skin (*see* 2.4.2: Eccrine Sweating), the decreased \bar{T}_{SK} cools the blood within the cutaneous vascular beds. Thus, metabolic heat is dissipated at the skin and cooled blood returns to the body core (Charkoudian 2003).

The maximal capacity by which the cutaneous circulation can vasodilate and increase blood flow is second only to that of skeletal muscle and, when healthy, maximal cutaneous vascular conductance is frequently achieved during instances of heat stress (Gonzalez-Alonso et al. 2008a). This increase in skin blood flow is enabled through an increase in cardiac output (Rowell et al. 1969a) and/or a vasoconstriction in the splanchnic and renal circulations (Rowell 1973; Rowell et al. 1970; Rowell et al. 1971), ensuring oxygen supply to vital organs is not compromised (Rowell 1974). These cardiovascular adjustments lead to a maximal skin blood flow of ~8 L/min (Gonzalez-Alonso et al. 2008a; Rowell 1974).

A reflex controlled increase in skin blood flow is mediated by an increase in T_C and continues until heat balance is achieved or maximal skin blood flow has been attained. This response provides negative feedback, such that as T_C is reduced, toward 'neutral' (or normothermia), skin blood flow returns to that occurring in a more moderate environment (Charkoudian 2003). There are distinct T_C thresholds at which a marked rise in skin blood flow occurs (Kenney and Johnson 1992). Beyond this activation threshold, the skin blood flow response is additionally characterized by the extent of increase in skin blood flow occurring with further increases in T_C , i.e. sensitivity (Charkoudian 2003). Alterations in either the threshold or the sensitivity to increases in T_C substantially impact the level of skin blood flow and the capability to dissipate heat. Specific to this thesis, exercise alters the threshold for cutaneous vasodilation (Kenney and Johnson 1992; Kenney et al. 1990; Roberts et al. 1977), while heat acclimation alters the sensitivity of this response (Roberts et al. 1977).

Perhaps less applicable to instances of exercise is that of locally mediated cutaneous vasodilation. With direct regards for whole body temperature regulation, this process is responsible for maintaining heat balance within the thermo-neutral zone, and therefore occurs prior to a discernable change in T_C (Bregelmann and Savage 1997; Savage and Bregelmann 1996). Furthermore, the local control of skin blood flow also permits fine adjustments in heat exchange within a specific body segment (Charkoudian 2010).

2.4.1.1: Neural Command of Skin Blood Flow

Reflex Control of Skin Blood Flow:

As addressed below, the peripheral pathways controlling skin blood flow have been investigated in humans. However, given the inherent difficulties associated with human experimentation and the CNS, the central efferent neural pathways involved in controlling skin blood flow has been identified in rats, whereby tail cutaneous vascular conductance controls convective heat loss (Nagashima 2006). In accordance, cutaneous vasodilation is elicited from within the preoptic area via activation of warm thermo-sensors, rather than by the inhibition of cold thermo-sensors (Zhang et al. 1995b). The central control of skin blood flow is mediated by the activity of sympathetic vasoconstrictor nerve fibers (O'Leary et al. 1985), and the efferent pathway appears to descend from the preoptic area through the medial forebrain bundle (Kanosue et al. 1994) and the ventrolateral periaqueductal gray or the ventral trigeminal area (Zhang et al. 1997) within the midbrain. The latter pathways involving the ventrolateral periaqueductal gray and ventral trigeminal area are likely differentiated depending upon the signal being sent from the preoptic area. Hence, it appears that excitatory signals are sent via the periaqueductal gray while inhibitory signals are sent through the ventral trigeminal area (Nagashima 2006). These pathways converge and continue via the medullary raphe within the medulla oblongata (Tanaka et al. 2002). Notably, this region has been identified in humans as being actively related to skin blood flow responses (McAllen et al. 2006). The final relay within the CNS is within the intermediolateral cell column of the first or second lumbar segment in the spinal column (Smith et al. 1998) (Figure 2.7). After this point, the peripheral nervous system and other local factors are responsible for changes in cutaneous vascular conductance, many of which are presented in the following.

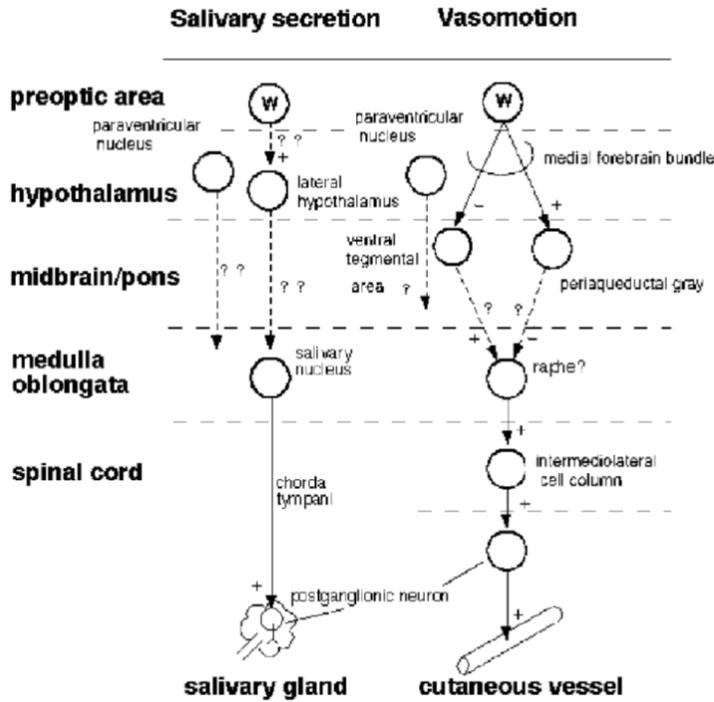


Figure 2.7: Efferent CNS autonomic heat defense neural pathways as demonstrated by Nagashima (2006).

More peripherally, the sympathetic adrenergic vasoconstrictor nerves and the sympathetic vasodilator nerves co-exist to control the reflex thermal responses of the cutaneous circulation. The vasoconstrictor system is tonically active in a moderate environment and is principally responsible for maintenance of normal body temperature with slight changes in activity or ambient temperature (Charkoudian 2003). However, when T_C becomes elevated the vasoconstrictor system only accounts for only ~10% of the cutaneous vasodilation, while the remaining ~90% of the increase in skin blood flow is mediated via activation of the sympathetic vasodilator nerves (Pergola et al. 1994).

The control of these sympathetic components is driven by the combined effects of changes in both \bar{T}_{Sk} and T_C . The sympathetic vasoconstrictor nerves release norepinephrine which binds with the postsynaptic α_1 - and α_2 - receptors in the cutaneous vasculature (Charkoudian 2003). During heat stress it is the inhibition of the

release/receptor uptake of norepinephrine which mediates vasodilation of the cutaneous vascular beds. Likewise, active vasodilation via the sympathetic vasodilator nerves is mediated by sympathetic cholinergic nerve transmission (Charkoudian 2003). Further, there is a moderate role for nitric oxide in the active vasodilatory response as nitric oxide contributes ~15% of the vasodilation response to whole body heat stress (Kellogg et al. 1998).

Local Control of Skin Blood Flow:

In addition to changes in \bar{T}_{sk} and T_C , local skin temperature contributes importantly to the control of skin blood flow, and as expected local warming of the skin results in a substantial cutaneous vasodilation (Charkoudian 2003). This vasodilation response to local heating is bi-phasic, and is characterized by an initial rapid increase in blood flow for the first 3-5 min, which is then followed by a moderate decline and later a moderate, slow, increase in vasodilation that attains a plateau after 25-30 min of warming, with the final level of cutaneous vasodilation being proportional to the local temperature of the skin (Pergola et al. 1993) (Figure 2.8).

The initial rapid vasodilation during local warming is primarily mediated by the local activity of thermo-sensors in the skin (Stephens et al. 2001), and occurs independent of an intact adrenergic system (Pergola et al. 1993). Further, the second vasodilation phase has been shown to rely on the local production of nitric oxide, and as could be expected this nitric oxide dependent rise in cutaneous vasodilation and skin blood flow is abolished when nitric oxide synthase is inhibited (Minson et al. 2001).

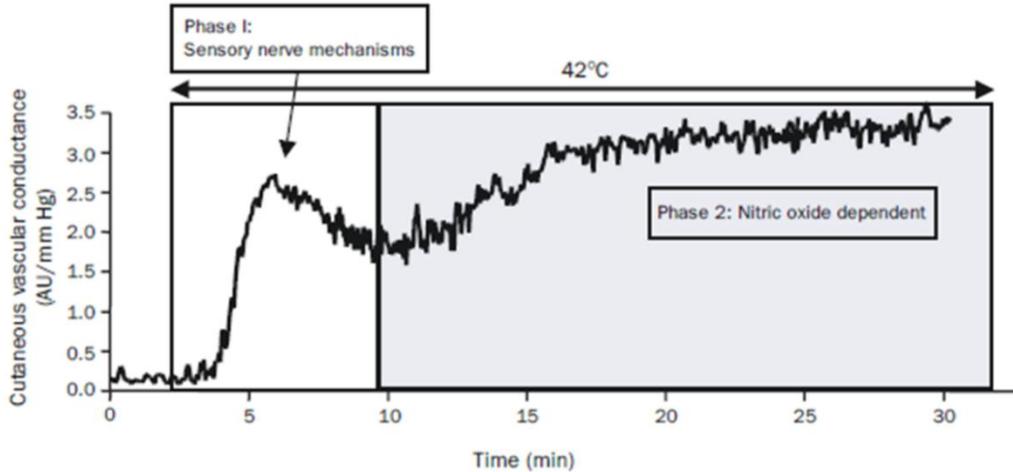


Figure 2.8: Typical cutaneous vasodilation of local warming. The initial rapid peak (Phase 1) is due to local sensory nerve activity, whereas the slower phase (Phase 2) depends on nitric oxide (Charkoudian 2003).

It is certainly notable that these descriptions of the reflex and local control of skin blood flow are very introductory. However, it is out of the scope of this thesis to inclusively and critically review these topics. Nevertheless, both of these control systems significantly contribute to temperature regulation during instances of both rest and exercise, and within and outside of the thermo-neutral zone. However, the control of these responses, specifically reflex control, can be modified by various non-thermal factors. Those non-thermal factors relevant to this thesis are addressed below.

2.4.1.2: *Non-Thermal Modulation of Skin Blood Flow*

Exercise initiates a nearly body wide vasoconstriction in order to direct cardiac output to the metabolically active muscles (Rowell 1974). Thus, the commencement of exercise is accompanied by a non-thermal vasoconstriction within the cutaneous circulation. Consequently, during exercise under heat stress skin blood flow is immediately reduced upon the initiation of exercise, even despite elevations during the rest period preceding exercise (Johnson and Park 1982). While the net skin blood flow response to continued dynamic exercise is that of vasodilation (Kenney and Johnson 1992), the characteristics

of the vasodilation response are non-thermally affected by exercise. For instance, the onset of cutaneous vasodilation is increased to a higher T_C during exercise when compared to that occurring during passive heating (Kellogg et al. 1991a). This response is graded and dependent upon exercise intensity with the threshold for the onset of cutaneous vasodilation increasing as exercise intensity increases (Taylor et al. 1988). Likewise, maximal skin blood flow is ~50% lower during exercise than that observed at rest, despite the additional increases in T_C (Kellogg et al. 1993).

In continuance, relative to passive heating, the non-thermal effects of exercise on the cutaneous circulation are: 1.) An attenuated vasodilation at the onset of exercise; 2.) An elevated T_C threshold for cutaneous vasodilation; and 3.) A decreased maximal skin blood flow (Figure 2.9). All of these responses appear to be mediated by different mechanisms. For instance, the cutaneous vasoconstriction that occurs at the onset of exercise is modulated by the adrenergic vasoconstrictor system (Kellogg et al. 1991b), while the active vasodilator system accounts for the elevated T_C threshold (Kellogg et al. 1991a). The active vasoconstrictor system is also responsible for the reduced maximal skin blood flow, as exercise effectively limits the active vasodilator system independent of vasoconstrictor activity (Kellogg et al. 1993). Thus, it is apparent that heat loss is not the initial priority during exercise in the heat. Rather, it appears as though cardiac output is preferentially directed to the working muscle at the expense of the thermoregulatory system at the onset of exercise, even despite the thermal load that exercise places on the body.

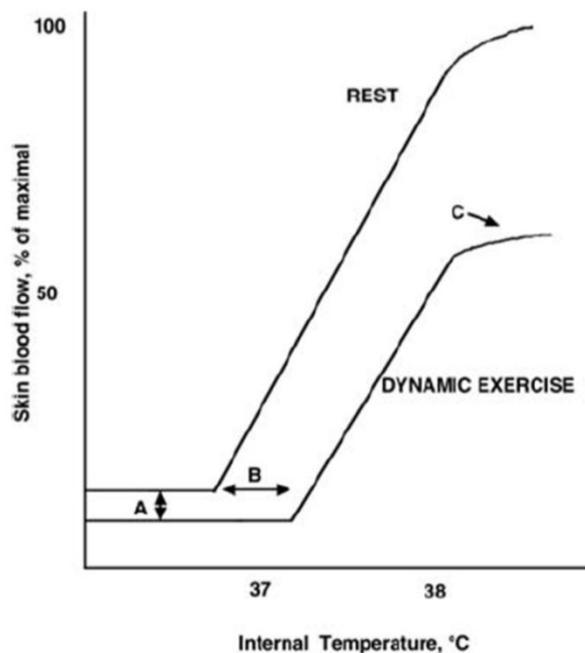


Figure 2.9: Schematic description of the thermoregulatory control of skin blood flow as modified by moderately intense exercise. The relation of skin blood flow to internal temperature (i.e. T_C) is affected relative to resting conditions, in at least three ways by exercise: a vasoconstrictor response at the onset of dynamic exercise (A), an increase in the internal temperature threshold at which skin blood flow begins to increase (B), and a leveling off in skin blood flow above an internal temperature of 38°C at a level well below maximal (C). Exercise exerts these effects through the vasoconstrictor system for the initial vasoconstriction and through inhibiting the active vasodilator system for the increased threshold and for the plateau. At rest, the plateau only occurs as skin blood flow approaches maximal vasodilation (Gonzalez-Alonso et al. 2008a).

The regulation of body fluids also non-thermally modulates the cutaneous blood flow response. Maximal skin blood flow is attenuated during instances of plasma hypovolemia, without regard to plasma osmolality (Fortney et al. 1984; Nadel et al. 1980) while hypervolemia has no benefit beyond isovolemic conditions (Nadel et al. 1980). Further, plasma osmolality has been shown to affect the T_C threshold for the onset of cutaneous vasodilation such that hyperosmotic conditions have been demonstrated to elevate this threshold (Fortney et al. 1984; Nadel et al. 1980). However, there are

discrepancies in the literature when it comes to the influence of plasma volume and osmolality on the sensitivity of the skin blood flow response; these appear to stem from differences in experimental protocol (Kenney and Johnson 1992). Nevertheless, given the evidence available, plasma hypovolemia appears to decrease the sensitivity of the skin blood flow response (Fortney et al. 1981; Fortney et al. 1984) (Figure 2.10). Due to sweat losses, prolonged exposure to heat stress and/or exercise can result in substantial dehydration. Dehydration is characterized by plasma hypovolemia and hyperosmolality, which impairs all aspects of the control of skin blood flow.

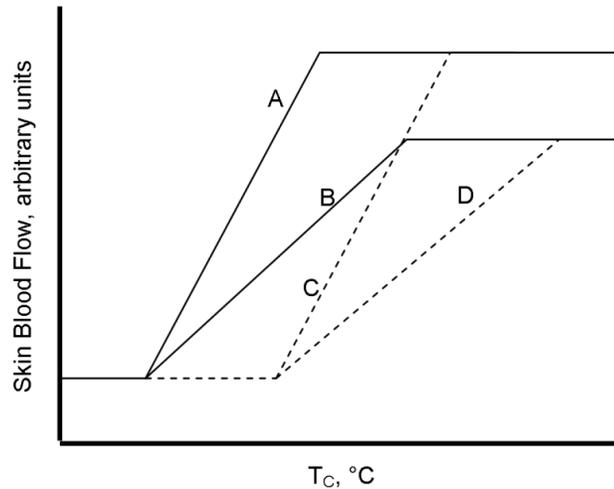


Figure 2.10: Schematic of control of skin blood flow as modified by plasma volume and osmolality under four conditions. A, iso-osmotic, isovolemic; B, iso-osmotic, hypovolemic; C, hyperosmotic, isovolemic; D, hyperosmotic, hypovolemic.

2.4.2: Eccrine Sweating

Sweating involves the secretion of fluid onto the surface of the skin and specific to thermoregulation this fluid (or sweat) provides the medium for evaporative heat loss. When the gradient between \bar{T}_{SK} and ambient temperature becomes reduced heat dissipation via radiation and convection are minimized (Taylor 2006), and in these instances temperature regulation is reliant primarily upon the evaporation of sweat, which

is driven by the water vapor pressure gradient between the skin and the ambient air (Nadel 1979). As such, increases in sweat rate (up to 100% skin wettedness) cause an increase in the water vapor pressure at the skin, thereby increasing the skin to ambient air vapor pressure gradient, promoting an increase in evaporative heat loss. Thus, sweat rate is an autonomically controlled thermoregulatory heat loss response.

There are two types of sweat glands in the human body, apocrine and eccrine. Apocrine glands are associated with hair follicles, while eccrine glands are characterized by ducts that independently spiral through the epidermis (Robertshaw 1977). Apocrine glands exist primarily under the arms and in the genital region and do not generally serve a thermoregulatory function. By contrast, eccrine glands primarily provide the sweat needed for evaporative heat loss. Eccrine glands are tubular structures that consist of a bulbous secretory coil, that secretes sweat, and a duct portion that passes through the dermis and exudes sweat onto the surface of the skin (Shibasaki et al. 2006).

Upon neural stimulation of the eccrine gland, the secretory bulbous secretes an isotonic precursor fluid that is similar in composition to plasma, but without plasma proteins, into the duct portion of the gland. As this fluid moves through the secretory duct, towards the surface of the skin, most of the sodium and chloride are re-absorbed resulting in a hypotonic fluid (relative to plasma osmolality) being secreted onto the skin (Shibasaki et al. 2006). Although there is re-absorption, electrolyte balance may still be compromised due to sweating. Accordingly, loss of electrolytes in sweat is predominantly dependent upon sweat rate and the level of heat acclimation, while independent of metabolic rate, \bar{T}_{sk} , T_C , and age (Dill et al. 1938; Dill et al. 1966).

The combination of the number of sweat glands activated and the amount of sweat released per gland comprises sweat rate (Shibasaki et al. 2006). The increase in sweat rate is biphasic such that the initial increase in sweating is mediated by the number of sweat glands activated, while further increases in sweat rate are driven by the amount of sweat per gland. Sweat gland recruitment responds rapidly and becomes maximal within ~8 min of the commencement of exercise in the heat, while sweat output per gland is

achieved gradually throughout the duration of the heat stress (Kondo et al. 2001). Thus, after ~8 min any increase in sweating is mediated by the increase in sweat output per gland (Kondo et al. 2001). This biphasic increase in sweating allows for average maximum sweat rates of ~1.4 L/h (Gerking and Robinson 1946). However, maximal sweating cannot be maintained indefinitely and, as such, decreases in the rate of sweating have been observed after 4 – 6 h of heat exposure despite sustained elevations in T_C (Gerking and Robinson 1946), i.e. hidromeiosis (Kerslake 1972). The precise mechanisms responsible for this decreased sweating rate with prolonged exposure to heat are currently unknown. However, both central (dehydration: hypovolemia and hyperosmolality) and peripheral (prolonged skin wettedness) factors have been suggested (Kerslake 1972; Shibasaki et al. 2006).

2.4.2.1: Neural Command of Sweating

Similar to that of skin blood flow, the central neural pathways involved in controlling evaporative heat loss have attempted to be elucidated using a rat model. Under this paradigm evaporative heat loss is mediated by the spreading of saliva on the fur, an autonomic thermoregulatory response (Nagashima 2006). In accordance, it is well established that warming of the preoptic area increases salivary secretion (Kanosue et al. 1990; Nakayama et al. 1986). However, links between the preoptic area and the medullary salivary neurons remain unclear (Nagashima 2006) (Figure 2.7). Although the experimental rat model has provided a valuable contribution to the mapping of thermoregulatory CNS pathways, the transferability of this relatively unknown salivary pathway, to evaporative cooling pathways in humans is highly questionable. Given that there are very few appropriate non-human experimental models enabling identification of the central pathways mediating eccrine sweating, it is apparent that little is known concerning the central control of this thermo-effector.

Peripherally, eccrine (sweat) glands are largely innervated by sympathetic cholinergic nerves and upon increases in \bar{T}_{SK} and/or T_C activation of the gland ensues. The stimulation of the sweat glands is controlled by the release and binding of acetylcholine, along with a peptide neuromodulator, from the cholinergic nerves on the muscarinic

receptors on the eccrine sweat gland (Shibasaki et al. 2006). Although thermoregulatory sweating primarily occurs via stimulation of the muscarinic receptors (Shibasaki et al. 2006), catecholamines, particularly epinephrine, also play a role both centrally and locally in the stimulation of sweat secretion. Hence, high local concentrations of catecholamines, acting on α -receptors (Uno and Hokfelt 1975), and blood-borne catecholamines, stimulating β -receptors (Sato 1973), can also increase sweating. Further, exercise and dehydration may also be important non-thermal modulators of the sweating response (Shibasaki et al. 2003a).

2.4.2.2: Thermal Control of Sweating

Thermal sweating is modulated by both local and central mechanisms. However, this response is mediated in a markedly different manner than that of skin blood flow. Central control is mediated by changes in \bar{T}_{sk} and/or T_C , and thus can be characterized by a threshold T_C (at a given \bar{T}_{sk}) and the sensitivity to further increases in T_C (Shibasaki et al. 2006). The onset of sweating is said to be driven by central sweating drive. This central drive can be adjusted acutely via changes in \bar{T}_{sk} such that an elevated \bar{T}_{sk} results in a lower threshold for the onset of sweating while a decrease raises the threshold (Figure 2.11) (Nadel et al. 1971). Central sweating drive can also be adjusted chronically by heat acclimation (Nadel et al. 1974; Shibasaki et al. 2006) and microgravity exposure (Shibasaki et al. 2006). By contrast, changes in the sensitivity of the sweating response indicates changes at the level of the sweat gland, and this has been shown to be affected by physical fitness level (Nadel et al. 1974) and dehydration (Montain et al. 1995).

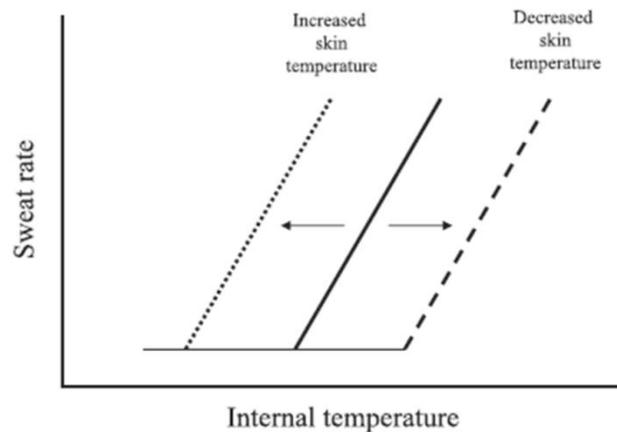


Figure 2.11: Effect of mean skin temperature on the relationship between sweat rate and internal temperature. Initially, as internal temperature increases, sweating does not occur. However, after a threshold is surpassed, the increase in sweat rate parallels the rise in internal temperature, and this threshold can be shifted by mean skin temperature (Shibasaki et al. 2006).

When the centrally derived sweating response is constant (i.e. central sweating steady-state), sweat rate can also be influenced by the local temperature of the sweat gland such that local heating accentuates sweat rate, while cooling attenuates sweat rate (MacIntyre et al. 1968). Mechanisms for this alteration of the sweating response appear to be at the glandular level and may be a direct effect of temperature on neurotransmitter release (i.e. local heating increases the release of acetylcholine, while local cooling inhibits the release of acetylcholine) (MacIntyre et al. 1968), or sensitization or desensitization of the sweat gland receptors by temperature with local warm and local cooling respectively (Ogawa 1970).

2.4.2.3: Non-Thermal Modulation of Sweating

The control of sweating is based on the interactions between thermal factors both centrally and locally derived. However, it has also been found that there are non-thermal factors that mediate the sweating response. Although these non-thermal factors modulate a thermoregulatory response it is unclear as to whether their primary role is thermal in nature. Whatever part these factors play, exercise and dehydration (i.e. hypovolemia and

hyperosmolality) crucially influence the regulation of the sweating response (Shibasaki et al. 2003a; Shibasaki et al. 2006).

Independent of changes in core, muscle, venous blood or skin temperatures, sweating occurs within ~2 s with the onset of dynamic exercise (Gisolfi and Robinson 1970). In accordance, exercise serves as a non-thermal modulator of sweating. Two mechanisms have been shown to control the non-thermal effects of exercise on the sweating response. The first is derived via impulses from the motor cortex which are irradiated by the CNS (Shibasaki et al. 2003b). When this central command (Goodwin et al. 1972) is enhanced it has been shown that the sweat rate is also enhanced (Shibasaki et al. 2003b). The second mechanism is derived from the mechano- and metabo-sensitive afferents that are responsible for evoking the exercise pressor reflex (Mitchell et al. 1983). Post-exercise ischemia isolates muscle metabo-receptor stimulation (Shibasaki et al. 2006) and when controlling for baroreceptor activation it has been demonstrated that the elevation in sweat rate is mediated by the activation of muscle metabo-receptors (Shibasaki et al. 2004). Exercise pressor reflex control of sweating is also mediated by muscle mechano-receptors (Shibasaki et al. 2004), although this response is not to the same magnitude as that elicited by metabo-receptors (Shibasaki et al. 2006).

Undoubtedly, future studies are needed to elucidate the specific non-thermal factors contributing to the sweat response at the onset of exercise (Shibasaki et al. 2006). Likewise, studies evaluating the interaction between thermally and non-thermally mediated sweating are also warranted, as the rationale behind why exercise non-thermally accelerates sweating is also not inherently clear. However, it is likely that the enhanced evaporative heat loss may combat the cutaneous vasoconstriction occurring at the onset of exercise, but at present this simply remains a hypothesis.

Prolonged exposure to heat stress and sweating can induce profound body fluid deficits. The resulting dehydration lowers both intracellular and extracellular volumes which results in plasma hyperosmolality and hypovolemia. Not surprisingly, the regulation of body fluids appears to impair the thermal sweating response (Shibasaki et al. 2006).

Relative to the euhydrated state, dehydration results in an elevated T_C during exercise at a given intensity (Montain and Coyle 1992). This elevated T_C was originally attributed to inadequate sweating (Greenleaf and Castle 1971). However, it has been proposed (Nadel 1979), and since demonstrated (Montain et al. 1995), that dehydration affects both the sensitivity of the sweating response to increases in T_C and the threshold for the onset of sweating. Further, this response is graded such that the change in the threshold and sensitivity of the sweating response is based on the level of dehydration (Montain et al. 1995).

More specifically however, plasma osmolality has been demonstrated to modulate the sweating response such that, the onset of sweating in the hyperosmotic condition is elevated to a higher T_C when compared to the iso-osmotic condition (Fortney et al. 1984). Likewise, hypovolemia reduces sweating sensitivity compared to isovolemia, but hypervolemia does not have an added sweating benefit beyond that of isovolemia (Taylor et al. 1988). Thus, the characteristic increase in the onset of sweating threshold and the reduced sensitivity observed during dehydration (Montain et al. 1995) can be independently attributed to the increase in plasma osmolality (hyperosmolality) (Fortney et al. 1984) and a decrease in fluid volume (hypovolemia) (Taylor et al. 1988) (Figure 2.12). Given these findings, it is evident that the body preferentially emphasizes the regulation of body fluids to the detriment of temperature regulation.

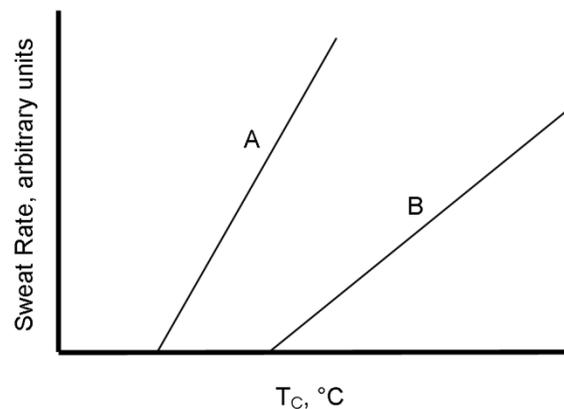


Figure 2.12: Schematic of control of the sweating response as modified by dehydration. A, normal (isovolemic, iso-osmotic); B, dehydration (hypovolemic, hyperosmotic).

2.4.3: Heat Acclimatization¹

Heat acclimatization is a phenotypic adaptive response whereby physiological thermoregulatory changes occur that reduce the strain a person experiences when repeatedly exposed to the stress of a naturally hot climate (Mercer 2001). Although they are etymologically indistinguishable, heat acclimation is an artificially-induced adaptation to heat without other climatic components (i.e. as occurs in a laboratory setting). Heat acclimatization improves exercise tolerance in the heat resulting in a reduced incidence and severity of heat illness and an enhancement in exercise performance (Armstrong 1998). Short-term acclimatization occurs in days to weeks whereas long-term acclimatization (habituation) usually occurs after years of exposure to a hot climate (Mercer 2001). Although it is not the focus of this thesis, heat acclimatization is an important physiological process modulating exercise tolerance in the heat. The following provides a brief overview of the adaptations associated with the abovementioned autonomic thermoregulatory responses mediating improvements in cooling capacity.

The primary stimuli for heat acclimatization are a sustained increase in T_C and sweating (Taylor 2000). Therefore, while passive heat exposure and exercise in a cool or moderate climate result in some benefit (Gisolfi and Robinson 1969), exercise in the heat is the most effective method of adaptation due to the combined exogenous (ambient) and endogenous (metabolic) heat loads (Nadel 1979). Heat acclimatization occurs quite rapidly as has it has been observed that 80% of the physiological adjustments occur within the first seven days (Robinson et al. 1943). Although, this rate depends on the duration and intensity of the exercise bouts, the physiological changes associated with heat acclimation persist regardless of the protocol.

The basic characteristics of heat acclimation are a decreased resting T_C and a decreased T_C at a given exercise intensity, both of which create a greater cooling capacity during the exercise bout (Brooks et al. 2005; Fink et al. 1975; Gisolfi and Robinson 1969; Nadel et

¹For simplicity purposes, acclimatization will be used to mean both acclimatization and acclimation.

al. 1974; Nielsen et al. 1993; Nielsen et al. 1997; Piwonka and Robinson 1967; Roberts et al. 1977; Robinson et al. 1943; Wyndham 1973). These responses are brought about by an enhanced physiological cooling capacity. Plasma volume is expanded due to an increased concentration of plasma proteins, and sodium and chloride retention (Nielsen et al. 1993; Nielsen et al. 1997). This affords a greater stroke volume, lower heart rate and a lower T_C threshold for skin blood flow (Nielsen et al. 1993; Nielsen et al. 1997; Roberts et al. 1977). These responses facilitate a more rapid transference of heat from the body core and active muscle to the periphery; thus, improving non-evaporative heat loss. Furthermore, the eccrine sweat gland is more active for a given T_C (i.e. increased sensitivity) (Nadel et al. 1974) and it reabsorbs more sodium and chloride (Dill et al. 1938), resulting in a greater efficiency of heat dissipation due to an increased water vapor pressure gradient between the skin surface and the ambient air (Hori 1995). An increased volume and more dilute sweat, especially when relative to (a reduced) T_C , enhances evaporative heat loss, which in turn reduces \bar{T}_{sk} , further improving non-evaporative heat transfer due to an increased core-to-skin temperature gradient. Quite briefly, it is in these ways that heat acclimatization improves the cooling capacity of the body under heat stress.

2.4.4: Thermoregulatory Behavior

Thermoregulatory behavior is a coordinated action establishing an optimal condition for heat exchange between the environment and the body (Mercer 2001). While typically viewed as a primitive thermoregulatory response (i.e. ectothermic) (Barber and Crawford 1979; Heath 1970), all animals employ this powerful thermoregulatory means. Compared to the autonomic thermoregulatory responses, behavioral capabilities are virtually unlimited in capacity, exceeding those of changes, for example, in metabolism (Benzinger 1969) or sweating (Figure 2.1). Thus, behavior represents the primary means by which T_C is regulated (Attia 1984) and is typically regarded as the ‘first line of defense’ in temperature regulation (Werner et al. 2008). It is obvious therefore that behavior plays a large role in temperature regulation.

The aim of this section is to organize, analyze, and critically evaluate the current body of literature on the control of thermoregulatory behavior during rest. Much of the research to date utilizes non-human animals as research subjects. However, this section aims to specifically address human thermoregulatory behavior. Hence, an emphasis will be placed on research conducted in homeotherms, specifically humans. Notably, there is some evidence for thermoregulatory behavior during exercise (Flouris 2010). However, this will be thoroughly addressed later in this chapter (*see* 2.5.5: Behavioral Control of Exercise Intensity), while the present sections will focus primarily on that behavior elicited during rest.

2.4.4.1: Thermal Control of Behavior

“Quite suddenly the limbs were extended... and the patient experienced a sensation of pleasure which could be described as ‘basking in the cold’ [but]... till that time, there had been acute consciousness of the cold, discomfort and flexing of the limbs (Barcroft and Verzar 1931).” Perhaps unknowingly, Barcroft and Verzar (1931) witnessed the interaction between the thermal and subjective controllers of thermoregulatory behavior when, immediately after a bout of shivering, the subject felt comfortable in a cold environment. Although T_C and \bar{T}_{Sk} were not continuously measured, a further drop in T_C was more than likely prevented by shivering, perhaps giving the perception of comfort and initiating thermoregulatory behavior (i.e. limb extension). Similarly, Carlton and Marks (1958) found that rats when exposed to cold ambient temperatures behaviorally worked for heat more often than rats that were exposed to a more moderate environment. Once again however, neither T_C nor \bar{T}_{Sks} were measured, leaving no answers as to what thermal inputs were behaviorally controlled. Nevertheless, as T_C is regulated (*see* 2.2.1: The Regulated Variable), it is reasonable to conclude from this observation that T_C is capable of controlling thermal behavioral responses.

Indeed, rectal temperature, a common index of T_C (Mercer 2001), has been shown to drive thermal behavioral responses in squirrel monkeys (Adair 1971). Interestingly however, the control of the same behavior was more precise when the temperature of the anterior hypothalamus was manipulated (T_{aHYP}). Thus, the T_{aHYP} , a more localized and

higher hierarchal T_C location, has been found to capably drive thermoregulatory behavior in squirrel monkeys (Adair 1970, 1971, 1977) and rats (Cabanac and Dib 1983; Satinoff 1964). Comparable results have been found in studies using humans. For example, Cabanac et al. (1972; 1971) have confirmed that changes in T_C are capable of modulating thermal behavior. In this paradigm, the subjects were seated in a water bath with their hand in a water perfused glove and were instructed to behaviorally maintain thermal pleasantness by adjusting the temperature of the glove. T_C and \bar{T}_{SK} were then altered to varying degrees by the temperature of the water bath. Behavioral reliance on T_C was illustrated by the findings that glove temperature was always adjusted opposite to that of the change in T_C . Similarly, Bleichert et al. (1973) found that in order to maintain thermal comfort, \bar{T}_{SK} was behaviorally reduced in order to counteract the rise in T_C . Collectively, T_C , as measured at various anatomical locations, capably drives thermal behavioral responses.

Given that behavior in the abovementioned experimental paradigms typically involved changing the ambient environment (Adair 1970, 1971, 1977; Bleichert et al. 1973; Cabanac et al. 1972; Cabanac et al. 1971; Cabanac and Dib 1983; Satinoff 1964) it is likely that \bar{T}_{SK} plays a role in the control of thermal behavior. This is perhaps best exemplified in that the magnitude of behavioral cooling or heating of T_C is affected by the ambient temperature, and thus \bar{T}_{SK} . For example, when the T_{aHYP} is reduced, the extent of heat seeking behavior in rats is inversely related to ambient temperature (Satinoff 1964). Furthermore, behavioral cooling of \bar{T}_{SK} and/or T_{aHYP} in rats can be modified by both raising the T_{aHYP} or ambient temperature (Cabanac and Dib 1983). Thus, feedback from both T_C and \bar{T}_{SK} modify behavior. This is further exemplified in the recent findings that mean body temperature, an arithmetic derivative of \bar{T}_{SK} and T_C , adequately dictates thermoregulatory behavior in humans (Flouris and Cheung 2008).

After observing that thermoregulatory behavior in a cold environment was elicited by a decrease in \bar{T}_{SK} , and that the drive for this behavior was to achieve a constant \bar{T}_{SK} , thereby

inhibiting any change in T_C , Weis and Laties (1961) suggested that T_C changes too slowly for it to be the primary thermal input initiating behavior. Thus, according to this proposal, when given the freedom to behave, \bar{T}_{SK} ultimately dictates behavior. Accordingly, when given the opportunity to behave, T_C – colonic temperature (Epstein and Milestone 1968) and T_{aHYP} (Carlisle 1968b) – in rats has been found to be regulated by behavior alone, indicating that changes in \bar{T}_{SK} initiated these responses independent of changes in T_C . In fact, \bar{T}_{SK} may carry two to three more times more weight in the initiation of thermoregulatory behavior in rats than T_C does (Corbit 1969). Evidence in humans corroborates these findings. For example, using the glove temperature paradigm mentioned previously, Cabanac et al. (1971) demonstrated that prior to a change in T_C , \bar{T}_{SK} elicited behavior such that the temperature of the glove was adjusted to oppose changes in \bar{T}_{SK} . More recently it was observed that human subjects voluntarily moved between a warm and a cool environment based on changes in \bar{T}_{SK} and that this behavior effectively regulated T_C (Schlader et al. 2009). From these findings it is apparent that, when given freedom to behave, thermoregulatory behavior is elicited primarily via changes in \bar{T}_{SK} .

The activation of autonomic thermoregulatory responses to thermal stress are principally dictated by a threshold T_C (Cabanac and Massonnet 1977), with \bar{T}_{SK} playing a more modulatory role. Given that changes in \bar{T}_{SK} appear to elicit behavior, buffering changes in T_C , it would seem sensible that thermal behavior would be initiated prior to autonomic thermoregulatory responses. Accordingly, Stitt et al. (1971) demonstrated that the behavioral responses of the squirrel monkey occurred within the thermo-neutral zone. Thus, indicating that when there is freedom for behavior, the squirrel monkey behaviorally avoided sweating or shivering. Similarly, under heat stress, rats have been found to inhibit changes in T_C , by preferentially cooling their periphery via behavioral means (i.e. showering), rather than via an autonomic response (i.e. saliva spreading) (Epstein and Milestone 1968). Together, these findings suggest that behavior is the preferred response and that this behavior minimizes the activation of autonomic thermoregulatory responses (Gordon 1985; Schmidt 1978). In humans, anecdotal

evidence suggests that behavior is the preferred mode by which temperature is regulated (Werner et al. 2008). However, research is needed to establish this relationship.

The controlling role of \bar{T}_{sk} and the prevention of autonomic thermoregulatory activation suggests that although the outcome is the same (i.e. T_C is regulated), the neurophysiological controllers and pathways may be distinctly different. Indeed, as reviewed earlier in this chapter (*see* 2.2.4: Afferent Thermoregulatory Pathways), although the peripheral afferent thermo-sensory pathway is similar, the autonomic and behavioral pathways diverge at the lamina I in the spinal cord (Figure 2.5) (Craig et al. 2001; Han et al. 1998). Thus, the CNS pathways are unique. The neural afferent pathway for autonomic responses terminates in the preoptic area, whereby the appropriate thermo-effector is elicited (Nakamura and Morrison 2008a, b). By contrast, the neural afferent pathway for behavioral thermoregulation (i.e. the thermal sensory pathway), bypasses the hypothalamus and terminates at various locations within the cortex (Figure 2.5) (Craig 2002).

These independent neural pathways are supported by earlier findings whereby disruption of autonomic temperature regulation did not substantially disturb the capacity to behaviorally regulate T_C . As such, when behavior is restricted and the autonomic thermoregulatory responses are abolished via lesions to the anterior hypothalamus the regulation of T_C fails in rats exposed to both hot and cold environments. However, when these same rats are given the freedom to behave in the same thermal environments, T_C is able to be capably regulated via behavioral means (Almeida et al. 2006b; Carlisle 1969; Lipton 1968; Satinoff and Rutstein 1970; Schulze et al. 1981). Although it is well established that the neural pathways and controllers are different for autonomic and behavioral temperature regulation, compared to that of autonomic thermoregulatory responses, relatively little is known concerning the neuroanatomy of thermal behavior (Nagashima 2006; Nagashima et al. 2000; Romanovsky 2007). Nevertheless, given the nature of behavioral responses, the efferent neurophysiological pathway(s) most likely these originate within the motor cortex or other areas of the brain associated with voluntary movement (Brooks et al. 2005).

2.4.4.2: *The Initiation of Thermal Behavior*

As described previously, behavior effectively ensures that a given animal remains within the thermo-neutral zone (Stitt et al. 1971). This thermo-neutral zone is a physiological construct defined relative to the autonomic thermoregulatory responses associated with elevations in metabolism and evaporative heat loss, and thus, can only be applied to endothermic animals. As thermal behavior is observed across the extant animal kingdom (Bligh 1998; Cabanac 1996a; Marino 2008; Satinoff 1996), it is perhaps best to define this zone in terms of thermal preference or comfort (Satinoff 1996). Thermal comfort is the subjective indifference to the thermal environment, with the zone of thermal comfort being defined as the range of thermal conditions in which the animal expresses indifference to the thermal environment for an indefinite period of time (Mercer 2001). Notably, thermal preference in non-human homeotherms assumes thermal comfort, which appears valid under most circumstances (Satinoff 1996). This definition implies that the animal is aware of thermal comfort and the avoidance of discomfort. In turn, a given level of thermal discomfort must be a pre-requisite for thermal behavior. Given this apparent relationship between perception, behavior and the physiological outcome of this behavior, using humans as the research subjects may provide valuable insights into the control of this behavior as we have the capability to provide subjective feedback.

Alterations in subjective thermal indices typically include both a hedonic (or affective) and a discriminative component. In thermal physiology, the hedonic sensation is usually that of comfort or pleasantness, while discriminative perceptions are those of thermal sensation. Not surprisingly, these two perceptions are inherently different. As defined previously, thermal comfort is subjective indifference with the thermal environment (Mercer 2001), while thermal sensation identifies the relative intensity of the temperature being sensed (Attia 1984). Quantification of both of these indices allows for identification of the combined sensations “which we have often experienced in the winter as ‘Pleasantly Warm’ and in the summer as ‘Pleasantly Cool’ (Gagge et al. 1967).” Notably however, comfort is different from pleasure. Thermal comfort occurs in a non-stressful environment, while pleasure occurs when one goes from an uncomfortable thermal condition to one that is more comfortable (McIntyre 1980; Satinoff 1996). For

example, when someone is uncomfortably hot and a region of their skin is cooled, the stimulus is deemed pleasant (Attia and Engel 1981; Mower 1976). Thus, pleasantness serves as an indication of a given stimuli's 'usefulness' to the body (Cabanac 1971, 1987, 1992, 2005). In regard to temperature regulation, a stimulus that is deemed thermally pleasant aims to restore thermal comfort (Attia 1984). Thus, thermal pleasantness is a useful perceptual tool, but thermal discomfort provides the motivation for behavior (Gagge et al. 1967; Satinoff 1996).

In behavioral studies utilizing human subjects thermal behavioral responses have been found to be preceded by changes in the perception of 'pleasantness' (Cabanac et al. 1972; Cabanac et al. 1971) and feeling 'too warm' or 'too cool' (Schlader et al. 2009). Hence, these studies experimentally demonstrate that the initiation of thermoregulatory behavior is preceded by a 'negative' affective sensation. Likewise, other studies using a behavioral paradigm in which the subjects were instructed to maintain thermal comfort suggest that a given quantity of thermal discomfort was incurred prior to the initiation of behavior (Bleichert et al. 1973; Flouris and Cheung 2008; Mekjavic et al. 2005; Yogeve et al. 2010; Yogeve and Mekjavic 2009). Thus, thermal behavior has been empirically demonstrated to be motivated by the avoidance of thermal discomfort - a negative hedonic sensation - and therefore the attainment and maintenance of thermal comfort, a positive (or neutral) affective sensation. Any thermal or non-thermal factor which modifies the zone of thermal comfort or places a given animal outside the zone of thermal comfort dictates behavioral temperature regulation (Satinoff 1996). Therefore, thermal (dis-)comfort is the variable ultimately mediating the decision to behave.

2.4.4.3: Thermal Modulation of Discomfort

Under most circumstances, thermal sensation is derived peripherally (i.e. \bar{T}_{sk}) and is driven by changes in the thermal environment. Thus, this discriminative component to thermal perception occurs independent of changes in T_c , and is therefore dependent upon \bar{T}_{sk} (Mower 1976; Yao et al. 2007; Zhang et al. 2010c). However, during thermal transients, \bar{T}_{sk} lags behind the perception of thermal sensation (Flouris 2010; Gagge et al.

1967) and it is in such instances that stronger relationships have been reported between ambient temperature and thermal sensation compared to \bar{T}_{Sk} (McIntyre 1980). Thus, thermal sensation provides the body with information concerning the ambient thermal environment. Given that the peripheral afferent pathways for thermal autonomic and sensory responses are similar (Figure 2.5) this feedback is likely also associated with autonomic thermoregulatory responses (Gagge et al. 1967). By contrast, thermal behavioral responses are elicited relatively independent from those autonomous responses, and thus thermal discomfort seemingly provides the motivation to behave (McIntyre 1980; Satinoff 1996).

Thermal (dis-)comfort is intimately related to the thermal environment, T_C , and \bar{T}_{Sk} (Attia and Engel 1981, 1982; Bleichert et al. 1973; Chatonnet and Cabanac 1965; Hardy 1970; Mower 1976; Yaglou 1927). In non-transient (uniform) thermal environments, at a normothermic T_C , thermal comfort is strongly related to thermal sensation (Gagge et al. 1971; Zhang and Zhao 2009). Thus, thermal (dis-)comfort is determined largely by \bar{T}_{Sk} (Bulcao et al. 2000; Gagge et al. 1967; Nakamura et al. 2008; Pellerin et al. 2004; Yao et al. 2007). Furthermore, the thermal and non-thermal peripheral (skin) activation of innocuous thermo-TRPs has been shown to directly influence thermal behavior, and therefore thermal (dis-)comfort, in non-human homeotherms (Bautista et al. 2007; Dhaka et al. 2002; Moqrigh et al. 2005; Tajino et al. 2007), thereby, further establishing the importance of peripheral thermal sensation in thermal (dis-)comfort and behavior.

This intimate relationship between thermal sensation and thermal (dis-)comfort appears valid only during thermal steady-states or when one goes from ‘comfortable’ to ‘uncomfortable,’ as a result of changes in thermal sensation (e.g. from neutral-to-cold, or neutral-to-warm) (Gagge et al. 1967; Zhang and Zhao 2009). During the latter transients, Gagge et al. (1967) found that irrespective of absolute body temperatures, comfort improved when the thermal environment permitted the return of body temperatures (i.e. T_C and/or \bar{T}_{Sk}) towards a physiological ‘neutral’ level. For example, during heating from ‘cold-uncomfortable’ (sensation-comfort), \bar{T}_{Sk} s that were previously perceived as ‘warm-

uncomfortable' were sensed as 'warm-comfortable.' These findings were later corroborated when the thermal pleasantness of a given thermal stimulus was found to be dependent upon the overall thermal status of the body (Attia and Engel 1981, 1982; Cabanac et al. 1972; Cabanac et al. 1971; Chatonnet and Cabanac 1965; Mower 1976). Thus, a given thermal stimulus produces positive affect when it corrects a deviation in body temperatures, and negative affect when it displaces body temperatures (further) from 'neutral' (Cabanac 1971, 1987, 1992, 2005).

As observed with regards to behavioral responses, \bar{T}_{sk} appears to be an adequate thermal controller of (dis-)comfort (Cabanac et al. 1971; Mower 1976; Yao et al. 2007). However, should T_C be displaced from normothermia, the affective nature of a given stimulus is directly related to the restoration of normothermia (Attia and Engel 1981; Cabanac 1971, 1987, 1992, 2005; Mower 1976). Accordingly, during passive heating and cooling, T_C and \bar{T}_{sk} have been demonstrated to be equally weighted as inputs modulating thermal (dis-)comfort (Bulcao et al. 2000). However, in order to maintain thermal comfort Bleichert et al. (1973) found that during exercise T_C was four times more important than \bar{T}_{sk} in mediating thermal behavior. While likely due to methodological differences, there is no general consensus on the relative contributions of T_C and \bar{T}_{sk} in the control of thermal (dis-)comfort. Nevertheless, both T_C and \bar{T}_{sk} appear to play a role in the hedonic responses to thermal stressors. However, prior to a change in T_C , \bar{T}_{sk} undoubtedly takes priority.

The perception of thermal sensation and/or (dis-)comfort is non-uniformly distributed throughout the body (Arens et al. 2006a, b; Cotter and Taylor 2005; Crawshaw et al. 1975; Nakamura et al. 2008; Pellerin et al. 2004; Yao et al. 2007; Zhang et al. 2010a; Zhang et al. 2004). Not surprisingly, this is perhaps best exemplified in the dominant role that T_C plays in the control of thermal discomfort, and therefore, behavior (Attia and Engel 1981, 1982; Cabanac et al. 1972; Cabanac et al. 1971; Mower 1976). As the goal of behavior is to regulate T_C , the behavioral modulation of thermal (dis-)comfort is

largely driven by changes in \bar{T}_{sk} (Bulcao et al. 2000; Frank et al. 1999; Gagge et al. 1967; Nakamura et al. 2008; Yao et al. 2007). Furthermore, although changes in local (skin) temperature elicit a different magnitude of local thermal (dis-)comfort depending on the body location (Arens et al. 2006a, b; Cotter and Taylor 2005; Crawshaw et al. 1975; Nakamura et al. 2008; Pellerin et al. 2004; Yao et al. 2007; Zhang et al. 2010a; Zhang et al. 2004), whole-body affective sensations are responsible for the initiation of thermal behavior (Nakamura et al. 2008). Thus, it is notable that whole-body thermal sensation and thermal (dis-)comfort is strongly dictated by those parts of the body that pose the greatest thermal sensation and discomfort (Arens et al. 2006a, b; Yao et al. 2007; Zhang et al. 2010b) (Figure 2.13). In a given environment this would be that location of the body that is the warmest/coolest and most uncomfortable. In the cold, this is primarily driven by the local temperature and sensations derived from the extremities (Arens et al. 2006a, b; Wang et al. 2007; Yao et al. 2007; Zhang et al. 2010b), while in heat it is associated with sensations derived from the head and neck regions (Arens et al. 2006a; Yao et al. 2007; Zhang et al. 2010b) (Figure 2.13). These findings compliment other research indicating that in the heat the head and neck are the most perceptually sensitive body segments to cooling (Cotter and Taylor 2005; Crawshaw et al. 1975; Nakamura et al. 2008), yet are in contrast to the finding that the trunk is the most sensitive site to warming in the cold (Nakamura et al. 2008). However, the hands and feet were not evaluated in this experimental paradigm (Nakamura et al. 2008).

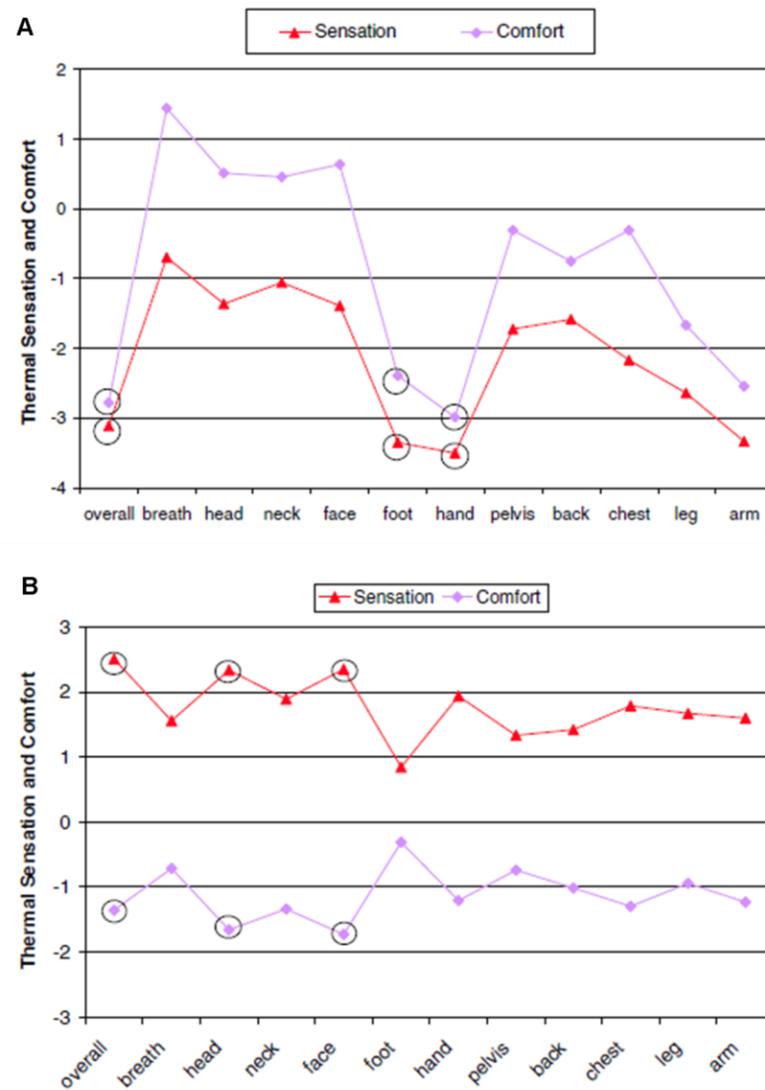


Figure 2.13: Local and overall thermal sensation and (dis-)comfort in a uniform cold (A) and warm (B) environment (Arens et al. 2006a).

2.4.4.4: Non-Thermal Modulation of Discomfort

Given the relationships between body temperatures and autonomic temperature regulation, it is notable that thermal (dis-)comfort is not likely to simply be a function of absolute body temperatures alone. In fact, cold discomfort and warm discomfort are directly influenced by shivering and sweating (Hardy 1970). Interestingly, although the

involuntary muscular activity associated with shivering is usually deemed uncomfortable (Hardy 1970), the associated increase in metabolic heat production inhibits the drop in T_C , improving thermal comfort (Barcroft and Verzar 1931; Hardy 1970). Under heat stress, discomfort increases. However, due to the cooling effect of the evaporation of sweat, \bar{T}_{sk} is probably not the sole determinant of thermal discomfort (Gagge et al. 1969; Hardy 1970; Winslow et al. 1937). The activation of sweating does not directly cause discomfort (Gagge et al. 1971). Therefore, it is more likely that the accumulation of non-evaporated sweat on the skin (i.e. skin wettedness) that negatively affects thermal comfort in hot conditions (Fukazawa and Havenith 2009; Gagge et al. 1969; Winslow et al. 1937).

The abovementioned relationships are most certainly notable, especially with direct regard for modeling thermal comfort (Gagge et al. 1971), but may not be directly applicable to the control of human thermoregulatory behavior during rest. As mentioned previously, when an animal is given freedom to behaviorally thermoregulate, it regulates its body temperatures within the thermo-neutral zone (Stitt et al. 1971) and this behavior prevents substantial increases in metabolic heat production and evaporative heat loss (Gordon 1985; Schmidt 1978). Thus, it would appear unlikely that thermal discomfort associated with shivering and/or skin wettedness dictates thermal behavior under most circumstances. Indirect evidence for this arrangement may be observed during instances of mild narcosis. Mild narcosis reduces the threshold for shivering during cold exposure in humans (Cheung and Mekjavic 1995; Mekjavic et al. 1994; Mekjavic and Sundberg 1992) and, consequently, is accompanied by less cold thermal discomfort for a given reduction in T_C (Cheung and Mekjavic 1995; Mekjavic et al. 1994; Yogev and Mekjavic 2009). However, the behavioral maintenance of thermal comfort remains unaffected (Yogev and Mekjavic 2009). Hence, under these circumstances widening of the thermo-neutral zone does not appear to alter the behavioral maintenance of thermal comfort in humans.

Tonically active within the thermo-neutral zone (and/or the zone of thermal comfort) is that of cutaneous vascular conductance, or skin blood flow (Bregelmann and Savage

1997; Ivanov 2006; Savage and Brengelmann 1996). Given their similar dependence on local (skin) temperature, \bar{T}_{sk} and T_C , it would appear likely that changes in skin blood flow may play a yet unidentified role in thermal sensation and (dis-)comfort. Accordingly, skin conductance (an indirect measure of skin blood flow), has been carefully not discounted as a potential factor mediating thermal discomfort (Gagge et al. 1969; Hardy 1970). For instance, cutaneous vasodilation has been proposed to directly increase sensation of warmth, while cutaneous vasoconstriction creates large temperature gradients within the skin, leading to the extremities feeling colder than the rest of the body (Hardy 1970). Likewise, providing perhaps the most direct evidence for skin blood flow as a modulator of thermal (dis-)comfort to date, the forearm-to-finger local (skin) temperature difference, an indicator of cutaneous vasoconstriction (Rubinstein and Sessler 1990), has been found to be related to sensations of cold and discomfort (Wang et al. 2007).

Although direct evidence is needed, there may be some indirect evidence for skin blood flow as a modulator of thermal (dis-)comfort and behavior. For instance, the perception of thermal sensation (Collins et al. 1981; Taylor et al. 1995) and reflex and local cutaneous vascular responses (Holowatz et al. 2007; Kenney 2001) are altered with age, and indeed there is some indication that thermal behavior is similarly modified (Crowe and Moore 1974; Taylor et al. 1995; Terrien et al. 2010). Likewise, observations during acute hypoxia in non-human animals nearly unanimously elicit behaviorally induced hypothermia compared to when they are normoxic (Wood 1991). This suggests that the zone of thermal comfort is shifted under hypoxic conditions (Satinoff 1996). Indeed, acute systemic hypoxia in humans negatively modifies cutaneous blood flow responses (Simmons et al. 2010; Simmons et al. 2007), thereby accelerating T_C cooling in the cold (Johnston et al. 1996). Acute mild hypoxia in humans has therefore been demonstrated to increase the cutaneous threshold temperature for the sensation of cold (Golja et al. 2004). However, apparently contradicting data suggests that the zone of thermal comfort (Golja et al. 2005), and thus behavior (Golja and Mekjavic 2003), are unaffected by hypoxia. In light of the data presented in non-human animals, these results are surprising and therefore warrant further investigation. However, these rather puzzling results are

remarkably similar to those obtained following prolonged horizontal bed rest, an experimental model for prolonged microgravity exposure. Following prolonged horizontal bed rest T_C is elevated (Crandall et al. 1994; Lee et al. 2002; Yogev et al. 2010), likely due to a relative cutaneous vasoconstriction (Crandall et al. 1994) and reduced maximal skin blood flow (Crandall et al. 2003). Likewise, autonomic warm (Crandall et al. 1994; Crandall et al. 2003; Lee et al. 2002) and cold (Mekjavic et al. 2005) responses are also impaired, widening the thermo-neutral zone. Furthermore, cool water immersion was found to be perceived as warmer and less uncomfortable with bed rest (Mekjavic et al. 2005), supporting previous work indicating a widening of the thermal comfort zone during adaptation to prolonged bed rest (Fortney et al. 1996). Interestingly however, prolonged bed rest has no effect on the behavioral maintenance of thermal comfort (Yogev et al. 2010).

To date, the relationships between autonomic temperature regulation, thermal perception and behavior are mixed, and any connections in humans are purely circumstantial. Hence, further research is needed in order to establish a relationship between factors altering both autonomic and behavioral responses in humans. Of particular importance may be the role of skin blood flow, and even more specifically, locally controlled skin blood flow, which is constantly active within the thermo-neutral zone (Bregelmann and Savage 1997; Savage and Bregelmann 1996). Thus, any factor that alters the local control of skin blood flow may, in turn, affect thermal behavior. This hypothesis may explain why behavior is modified with aging, but not during instances of hypoxia. For instance, aged persons have impaired local *and* reflex controlled skin blood flow responses (Holowatz et al. 2007) and similarly diminished behavioral responses (Crowe and Moore 1974; Taylor et al. 1995; Terrien et al. 2010). By contrast it is currently unclear as to whether alterations in skin blood flow associated with hypoxia are locally or reflexively mediated (Simmons et al. 2007). That thermal behavior is not affected by hypoxia (Golja and Mekjavic 2003) suggests that these skin blood flow responses are reflex in nature. An argument against this arrangement may be derived from the findings that prolonged bed rest reduces locally mediated maximal cutaneous blood flow (Crandall et al. 2003), yet has no effect upon the behavioral maintenance of thermal

comfort (Yogev et al. 2010). However, how changes in maximal skin blood flow affects local skin blood flow responses within the thermo-neutral zone remains uncertain.

At present there is clearly no evidence for or against the hypothesis that thermal behavior is modified and/or dependent on locally controlled skin blood flow. However, this proposal may be effectively mirrored by that of the control of sweat rate. For instance, sweat rate has been found to be influenced by *both* local temperature and skin blood flow (Wingo et al. 2010). As this is unlikely to be unique to only sweating, it would appear probable that other thermo-effectors are similarly dependent upon each other. Although this is perhaps not surprising, experimental evidence for this integrated arrangement is in its infancy, and further research is warranted.

Additionally, it currently remains uncertain as to whether a change in temperature is a requirement for the initiation of thermal behavior in humans. Rather, it is more likely that any factor inducing a change in thermal (dis-)comfort can dictate behavioral responses. An intriguing model for future research would be to activate peripheral innocuous cool and warm sensors, and monitor human thermal behavior. This non-thermal thermo-sensor activation has successfully modified behavior in rats (e.g. Bautista et al. 2007; Moqrich et al. 2005; Peier et al. 2002; Tajino et al. 2007). However, human subjects provide the advantage of subjective feedback, which could perhaps help complete our understanding of the ultimate manner by which human thermal behavior is controlled.

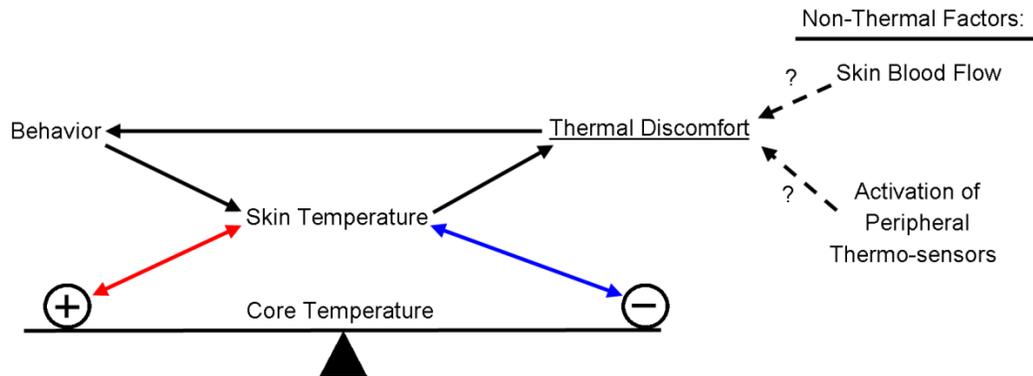
Finally, establishing experimental models sensitive enough to identify functional relationships between thermal (and non-thermal) stressors, and thermal behavior also warrants investigation. This is especially apparent considering that modification of the thermal comfort zone has not been found to affect the behavioral defense of thermal comfort (Yogev et al. 2010; Yogev and Mekjavic 2009). Notably however, these results could be attributed to the abovementioned local versus reflex controlled skin blood flow alterations. Furthermore, while the overall understanding of the signaling inputs for thermal (dis-)comfort are well developed, how these are translated into behavioral

responses is less clear. This is perhaps an artifact of the difficulty in measuring behavioral responses in humans, which may be reflected in the relatively small number of studies evaluating the control of human thermoregulatory behavior. Thus, in order to arrive at a more complete understanding of the control of human thermoregulatory behavior, research establishing experimental models is merited.

In summary, thermal behavior appears to be elicited by the whole-body affective sensation of thermal discomfort. Thus, discomfort is the controlling variable. Therefore, any factor that modifies thermal discomfort will undoubtedly affect the manner in which temperature is behaviorally regulated (Satinoff 1996). T_C and/or \bar{T}_{Sk} are capable of affecting thermal discomfort. However, when given the freedom to behave, as occurs in most free-living situations, \bar{T}_{Sk} appears to dictate thermal behavioral responses, thereby maintaining heat balance. Notably however, local (skin) temperature plays a large role in the overall perception of thermal discomfort. Furthermore, non-temperature related factors also likely modify thermal discomfort. Within the thermo-neutral zone, when \bar{T}_{Sk} is the primary thermal input, preventing a change in T_C , these factors likely include the non-thermal activation of peripheral thermo-sensors and locally controlled skin blood flow. However, when heat balance is lost, and T_C becomes the primary behavioral input, the non-thermal factors likely contributing to thermal discomfort include shivering and skin wettedness. An overview of the manner in which temperature regulation mediates behavior is presented in Figure 2.14.

Control of Thermal Behavior during Rest

A



B

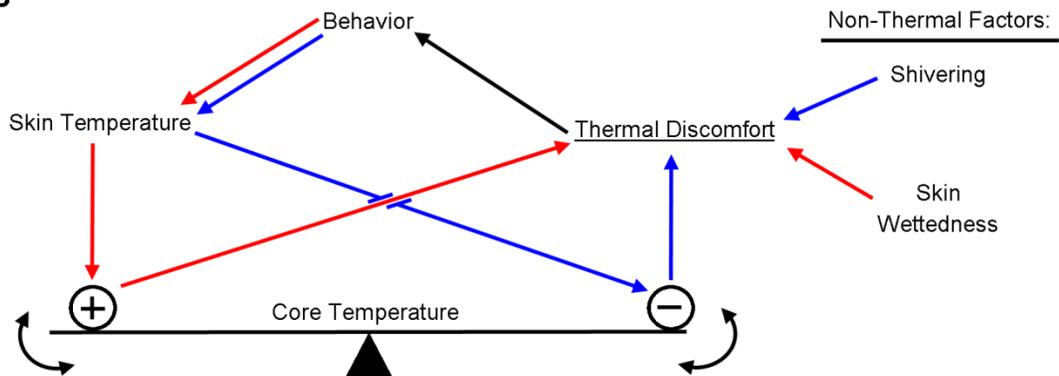


Figure 2.14: A schematic demonstrating the control of thermal behavior during rest when given freedom for thermoregulatory behavior (A) or when heat balance is lost (B). In both circumstances thermal discomfort is the controlling variable (denoted by: underline). In A, thermal behavior is mediated by \bar{T}_{sk} , thereby maintaining heat balance (i.e. heat gain (denoted by: +) = heat loss (denoted by: -)). However, locally controlled skin blood flow and/or the non-thermal activation of peripheral thermo-sensors also likely modify behavior. Should behavior be restricted or insufficient, heat balance can be lost (i.e. heat gain \neq heat loss; B). During these instances thermal discomfort is mediated by changes in T_C and shivering or skin wettedness. In most instances behavior alters the external thermal environment, and thus \bar{T}_{sk} , helping to restore T_C . Currently unknown pathways are denoted by a ? and a dashed line, while pathways mediated by heat gain and heat loss are denoted by red and blue lines.

At this point, the focus of this chapter will shift somewhat. In the following sections the fundamentals of human temperature regulation will be applied to that occurring during exercise in the heat. Specifically, this will entail how and why thermoregulation affects prolonged (endurance) exercise capacity and performance when undertaken in the heat. Additionally, it is hoped that by applying our knowledge of temperature regulation during rest to that during exercise some of the mechanisms dictating self-selected exercise intensity will become apparent.

2.5: Dynamic Exercise in the Heat

2.5.1: The Core Temperature Response

As presented, at rest T_C is well regulated by autonomic and behavioral capabilities, thereby ensuring heat balance nearly constantly. By contrast, during exercise, a transient rise in T_C occurs until autonomically derived heat balance is established (Webb 1995). As this point is approached the rise in T_C is attenuated, which occurs within ~20 min (Gant et al. 2004; Nielsen and Nielsen 1962, 1965; Saltin and Hermansen 1966). The resulting T_C plateau is achieved throughout a range of ambient temperatures (5°C - 30°C) (Nielsen and Nielsen 1962), and is predominantly a function of relative exercise intensity (Gant et al. 2004; Saltin and Hermansen 1966) and the thermal environment (Lind 1963). More specifically however, current evidence indicates the rise and subsequent plateau in T_C is a function of both the absolute exercise intensity, which dictates the rate of metabolic heat production, and relative exercise intensity, which modulates heat dissipation (Gonzalez-Alonso et al. 2008b).

The T_C response to exercise is not indicative of thermoregulatory failure (Nielsen and Nielsen 1962). Rather, it should be considered analogous to the elevation in mean arterial pressure (MAP) occurring during exercise, indicating that regulation does not always imply it must be maintained constant (Taylor et al. 2008). During uncompensable heat stress heat balance is impossible and T_C will continue to rise (Cheung et al. 2000). It is in these instances where increases in T_C (i.e. hyperthermia) may limit exercise tolerance in the heat (Cheung 2007a; Cheung and Sleivert 2004b; Gonzalez-Alonso et al. 2008a; Hargreaves 2008; Nybo 2008). This potential limitation will be discussed in many of the following sections.

2.5.2: Exertional Heat Illnesses

As has been thoroughly described in the preceding sections (*see* 2.4: Human Temperature Regulation and Heat Stress), exposure to hot environments places a large stress upon numerous physiological systems. It is in these instances where heat stress can develop into a heat illness, an array of medical conditions, some of which warrant emergency

care. Of specific interest to this thesis are those heat illnesses occurring during or as a result of exercise, exertional heat illnesses. Perhaps not surprisingly, exertional heat illnesses affect numerous physiological systems, ranging in severity from very minor to lethal, and are characterized by a wide range of signs and symptoms (Armstrong 2003). Notable exertional heat illnesses include, amongst others, potentially life threatening exertional heat stroke, heat exhaustion and heat cramps (Armstrong 2003; Armstrong et al. 2007; Binkley et al. 2002). It is out of the scope of this chapter to address the exertional heat illnesses in depth. However, the severity of instances in which temperature regulation can fail cannot be stressed enough, as this is the primary construct underlying thermoregulatory research. In the specific interest of this thesis, the following is a brief introduction to exertional heat stroke and heat exhaustion, and their apparent relationships.

Heat exhaustion is defined as the inability to continue exercising in a hot environment (Armstrong et al. 2007; Binkley et al. 2002). The signs and symptoms of heat exhaustion are neither specific nor sensitive (Armstrong et al. 2007), and vary widely amongst individuals (Armstrong et al. 1987). Frequent signs and symptoms include profuse sweating, dehydration, sodium loss, weakness, fainting, dizziness, headache, diarrhea, and nausea, amongst many others. Most importantly however, heat exhaustion is usually described by a $T_C < 40.0^\circ\text{C}$ (Armstrong et al. 2007; Binkley et al. 2002). This T_C threshold represents a cut-off point whereby, in addition to other signs and symptoms, exertional heat stroke is the likely diagnosis (Armstrong et al. 2007; Binkley et al. 2002).

It is therefore appropriate that heat stroke is considered the most dangerous of the exertional heat illnesses (Coris et al. 2004). The diagnosis of exertional heat stroke is described by extreme hyperthermia ($T_C > 40.0^\circ\text{C}$) and CNS changes (e.g. loss of consciousness, staggering, delirium, confusion, etc.) (Armstrong et al. 2007; Binkley et al. 2002). In contrast to that of heat exhaustion, the diagnosis of heat stroke represents a situation in which temperature regulation has failed (Bouchama and Knochel 2002; Coris et al. 2004). The pathophysiology of exertional heat stroke is directly mediated by overheating of body tissues inducing a combination of circulatory failures, endotoxemia,

and altered brain function (Binkley et al. 2002). The etiology of exertional heat stroke therefore includes significant cytokine, heat shock protein, and cell injury responses (Bouchama and Knochel 2002; Leon 2006). Although the precise origins of exertional heat stroke remain uncertain, it is well established that the length of time in which an individual remains hyperthermic profoundly affects the mortality rate (Leon 2006). Accordingly, aggressive cooling drastically improves survival from exertional heat stroke (Casa et al. 2007). By contrast however, it has been suggested that it is not body temperatures alone that dictate the outcome of exertional heat stroke (Noakes 2008). Rather, heat stroke may be mediated predominantly by factors intrinsic within a given individual, e.g. excessive endothermy (Rae et al. 2008), and perhaps treating the non-thermal physiological pathogenic responses, in addition to reducing body temperatures, would further improve the rate of survival (Noakes 2008). However, at present this remains only a proposal.

The progression from heat strain to heat stroke is not inherently clear (Bouchama and Knochel 2002). It has been suggested that thermoregulatory failure (i.e. heat stroke) simply represents the most serious of the heat illnesses, which can be viewed on a continuum of increasing severity as a function of the thermal load placed upon the body (Leon 2006). However, it remains to be seen as to whether a pre-requisite for exertional heat stroke is the development of another, less severe, heat illness. The most likely such scenario is the development of heat exhaustion prior to exertional heat stroke. Circumstantial support for this paradigm can be derived from the high incidence of exertional heat stroke when high motivation and external factors (e.g. a drill sergeant, coach, fellow runners, etc.) prevent individuals from ceasing exercise (or decreasing exercise intensity) when they approach exhaustion (Armstrong et al. 2007; Donoghue et al. 2000; Epstein et al. 1999; Shibolet et al. 1976), while a lower incidence of heat stroke, and other heat illnesses, has been reported when people exercise alone or self-pace (Brake and Bates 2000, 2002a). Although intriguing, direct evidence is required in order to establish that the cues signaling heat exhaustion are ignored *before* the development of exertional heat stroke.

2.5.3: Ambient Temperature and Exercise Performance

In addition to the thermal effects of exercise on body temperature regulation, dynamic exercise alone poses a formidable challenge to an array of regulatory systems. Therefore, it might be expected that the combined stressors of heat and exercise are additive, and therefore are capable of compromising exercise tolerance. Indeed, elevations in ambient temperature are associated with an increased percentage of non-finishers during prolonged running races (Vihma 2010; Wegelin and Hoffman 2011), while ambient temperature has also been found to be inversely related to exercise performance within a given competition (Ely et al. 2007a; Ely et al. 2007b; Ely et al. 2008; Vihma 2010; Wegelin and Hoffman 2011). Thus, the endogenous and exogenous thermal stress directly associated with exercise in the heat results in a relative exercise intolerance. The ultimate mechanisms for this reduced tolerance are currently unknown and remain a topic of intense research and debate within the fields of thermal and exercise physiology (Cheung 2007a; see reviews, Cheung and Sleivert 2004b; Gonzalez-Alonso et al. 2008a; Hargreaves 2008; Nybo 2008). The following is an outline and a critical (re-)analysis of the current state of knowledge concerning exercise tolerance and hyperthermia. Specifically, this will entail the effects, and potential mechanisms, of heat stress on maximal oxygen uptake ($\dot{V}O_2\text{max}$), time to voluntary exhaustion, and behavior during self-paced exercise. Given the nature of this thesis a particular emphasis will be placed on this latter component.

2.5.3.1: Maximal Oxygen Uptake

As presented previously (*see* 2.4.1: Cutaneous Vasodilation and Cardiovascular Adjustments), during passive heat stress the predominant whole body response is that of sympathetic vasoconstriction as it is necessary to distribute cardiac output to the skin for heat exchange. Accordingly, a modest reduction in blood flow to the muscle may ensue (Rowell 1974). During exercise, blood flow to, and oxygen uptake by, the working muscle must increase as a function of exercise intensity, with the magnitude of this increase being limited primarily by the ability of the heart to meet these demands, i.e. cardiac output (Gonzalez-Alonso and Calbet 2003; Gonzalez-Alonso et al. 2008a; Levine 2008). During exercise under heat stress the potential for cardiac output to be limiting is

compounded by the competition for cardiac output between the cutaneous and muscular circulations.

Heat stress generally has a negative effect on maximal (or peak) oxygen uptake, while the magnitude of this effect is mostly driven by the extent of body heating (Figure 2.15). For instance, independent of elevations in T_C , Rowell et al. (1969b) found peak oxygen uptake ($\dot{V}O_{2peak}$) to be marginally reduced (~3%) in the heat compared to $\dot{V}O_{2max}$ observed in the control trial. Likewise, Pirnay et al. (1970) found $\dot{V}O_{2peak}$ in the heat to be reduced by ~7%. However, pre-heating T_C further reduced $\dot{V}O_{2peak}$ in the heat by another 20% (Pirnay et al. 1970). Similarly, Saltin et al. (1972) found $\dot{V}O_{2peak}$ in the heat to be reduced by ~8% by pre-heating T_C . These findings have been generally corroborated (Arngrimsson et al. 2004; Arngrimsson et al. 2003; Dimri et al. 1980; Nybo et al. 2001; Sawka et al. 1985; Wingo et al. 2005), and it is nearly unanimous agreed (c.f. Williams et al. 1962) that heat stress reduces $\dot{V}O_{2peak}$. However, the extent of reduction in $\dot{V}O_{2peak}$ appears to be directly proportional to changes in body temperatures such that when only \bar{T}_{Sk} is elevated it is minimally affected, while when both \bar{T}_{Sk} and T_C are elevated the effect is magnified (Figure 2.15) (Arngrimsson et al. 2004; Arngrimsson et al. 2003).

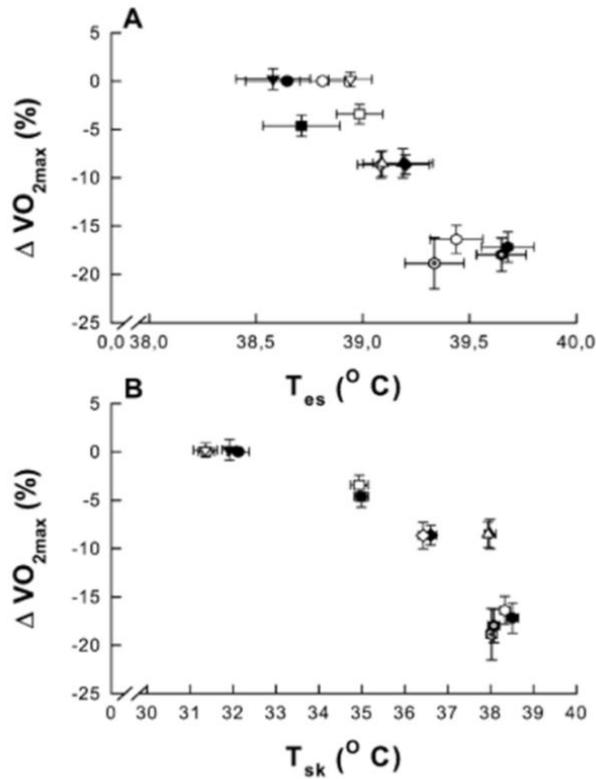


Figure 2.15: Relationship between changes in maximal (peak) oxygen uptake ($\Delta \dot{V}O_{2max}$) from the control condition ($25^{\circ}C$) and core temperature (T_{es} ; A) and mean skin temperature (\bar{T}_{sk} ; B) (Arngrimsson et al. 2004).

The rationale behind the observed reductions in $\dot{V}O_{2peak}$ in the heat is not readily apparent. It appears that the reduced oxygen consumption ($\dot{V}O_2$) at the point of voluntary exhaustion is due to a reduction in exercise intensity at exhaustion, and thus a submaximal $\dot{V}O_2$ is achieved. Evidence for this is depicted in Figure 2.16, where the reductions in $\dot{V}O_{2peak}$ occurring in the heat appear to be directly related to a reduction in exercise time, and therefore, under this incremental exercise protocol, a reduced exercise intensity at exhaustion (Arngrimsson et al. 2004). According to Brück and Olschewski (1987) this reduction in exercise tolerance in the heat can be adequately explained by a diminished drive to exercise in the heat, whereby increases in body temperatures together with the motivation to exercise, compromise exercise duration (Figure 2.17). Although

exercise motivation alone certainly plays a role, motivation is modulated by numerous physiological and perceptual factors (Figure 2.17). Specifically, when it comes to decrements in $\dot{V}O_{2\text{peak}}$ in the heat, a likely input is the competition for blood flow for thermoregulation and exercise (Rowell 1974). For instance, $\dot{V}O_{2\text{peak}}$ could be reduced directly due to a relative vasoconstriction in the working muscle, or indirectly via the inability to further increase cardiac output and the subsequent reduction in MAP (Rowell 1974).

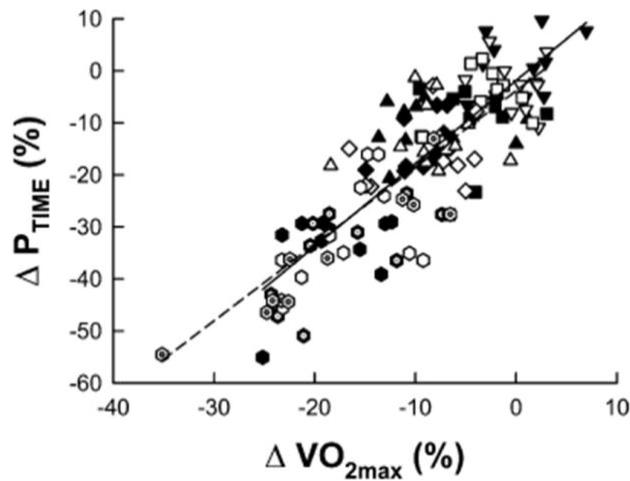


Figure 2.16: Relationship between the reduction in exercise time (ΔP_{TIME}) and the reduction in $\dot{V}O_{2\text{max}}$ (or peak) ($\Delta \dot{V}O_{2\text{max}}$) (Arngrimsson et al. 2004).

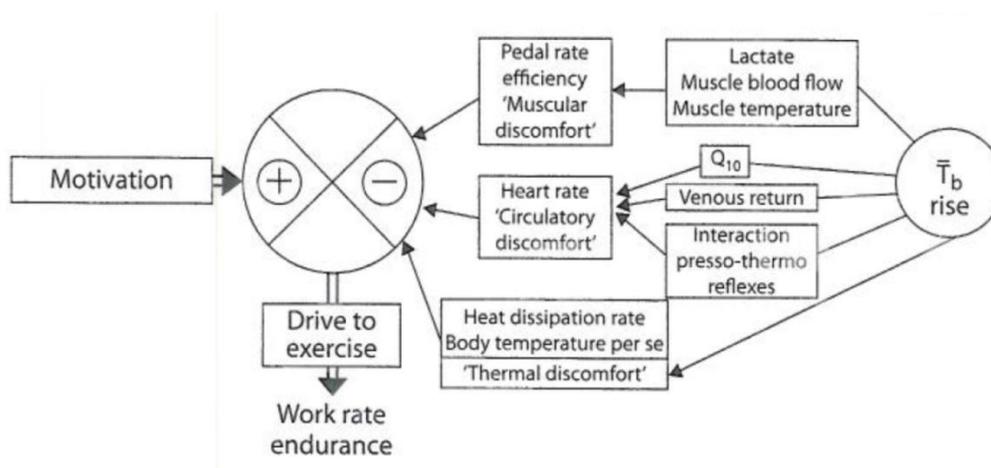


Figure 2.17: Factors by which body temperatures may exert their influence on exercise tolerance (Bruck and Olschewski 1987).

Rowell's hypothesis (Rowell 1974) for an indirectly limiting cardiac output was supported in an elegant study conducted by Gonzalez-Alonso and Calbet (2003) which identified the contributing factors that limits $\dot{V}O_{2\max}$ both with and without heat stress. Therefore, it was subsequently demonstrated that irrespective of the thermal status of the body, $\dot{V}O_{2\max}$ is dictated by the failure of the heart to maintain cardiac output. The corresponding drop in blood pressure subsequently reduced muscle blood flow, oxygen delivery and oxygen uptake (Gonzalez-Alonso and Calbet 2003). Hence, reductions in $\dot{V}O_{2\text{peak}}$ observed in the heat are not due to an active relative vasoconstriction at the muscle, but rather this (passive) physiological cascade was brought on much sooner in the heat. Therefore, through cardiovascular processes it appears likely that heat stress and temperature regulation indirectly have a negative impact on $\dot{V}O_{2\text{peak}}$, and perhaps sustainable exercise intensity and endurance (Gonzalez-Alonso et al. 2008a).

2.5.3.2: Heat Exhaustion

Although its impact is indirectly derived, given that heat stress negatively impacts $\dot{V}O_{2\text{peak}}$, at least in part, by reducing exercise tolerance time (Figure 2.16) (Arngrimsson et al. 2004), it can be reasonably speculated that exercise duration (e.g. time-to-exhaustion) might be negatively affected by hyperthermia. Indeed, MacDougall et al.

(1974) demonstrated that moderate intensity exercise duration was reduced with hyperthermia relative to when subjects were normothermic or hypothermic. Similarly, Galloway and Maughan (1997) found that exercise time-to-exhaustion was shortest in the heat, while Parkin et al. (1999) corroborated these findings by observing that moderate intensity exercise time-to-exhaustion was shortest in the heat, longer in moderate conditions, and longest in cool ambient conditions (Figure 2.18A). Thus, as could be expected, fixed-intensity (constant workload) duration is attenuated in the heat.

Historically, elevations in body temperatures have been hypothesized to directly reduce the tolerance to moderate intensity exercise in a range of homeothermic animals. For example, Dill et al. (1933; 1932) recognized that, during moderate intensity exercise when provided adequate energy and cooling, dogs were 'tireless.' However, as external temperature was increased, elevations in body temperatures drastically impaired exercise tolerance (Dill et al. 1933; Dill et al. 1932). Young et al. (1959) furthered these findings by demonstrating that exercise exhaustion in dogs was related to elevations in T_C , while Taylor and Rowntree (1973) keenly observed that cheetahs simply refused to run if T_{CS} were profoundly elevated. Likewise, elevations in T_C have been directly identified as factors limiting exercise performance in both goats (Caputa et al. 1986) and guinea-pigs (Caputa et al. 1985).

Similarly, evidence from exhaustive exercise in humans suggests that exercise duration is indeed mediated by elevations in T_C . This is supported indirectly in the abovementioned studies, whereby T_{CS} at exhaustion in the heat were consistently between 39.5°C and 40.0°C (Galloway and Maughan 1997; MacDougall et al. 1974; Parkin et al. 1999). These findings are reinforced by the observations that heat acclimation (Cheung and McLellan 1998; Nielsen et al. 1993), pre-exercise body temperature (Gonzalez-Alonso et al. 1999), the rate of heat storage (Gonzalez-Alonso et al. 1999) or hydration status (Cheung and McLellan 1998) do not modify the constancy of exhaustion in humans that occurs upon the attainment of a substantially elevated T_C . Subsequently, it was proposed that critically high T_C (~40°C) dictated heat exhaustion (Nielsen et al. 1993), which was supported by findings that rats became exhausted at startlingly consistent high T_C

irrespective of ambient (Fuller et al. 1998) and initial body (Walters et al. 2000) temperatures. As this temperature is below that associated with cellular damage (Hales et al. 1996), this phenomenon would therefore be advantageous preventing catastrophic hyperthermia (Cheung 2007a), i.e. exertional heat stroke.

As demonstrated in the Brück and Olschewski model (1987), elevations in body temperatures are not autonomous, and as such, are associated with a cascade of physiological responses (Figure 2.17). Thus, it is unclear as to whether exercise intolerance in the heat is directly associated with increases in T_C , or whether a T_C of $\sim 40^\circ\text{C}$ is an artefact of another physiologically limiting process. Accordingly, there is mounting evidence against a T_C of $\sim 40^\circ\text{C}$ limiting exercise performance. At rest, humans have been found to tolerate T_C temperatures in excess of 41°C without harm (Bynum et al. 1978; Dubois et al. 1981; Dubois et al. 1980). Likewise, T_C greater than 40°C have been observed during, and upon completion, of exercise without symptoms of exertional heat illness (Byrne et al. 2006; Lee et al. 2010; Maron et al. 1977; Pugh et al. 1967; Robinson 1963), while T_C approaching (Lee et al. 2010) or exceeding (Ely et al. 2009) this hypothetically critically high level have not been found to be deleterious to exercise performance during self-paced (variable intensity) running. Although a 'safety switch' terminating exercise prior to homeostatic failure is likely (Cheung 2007a; Cheung and Flouris 2009), there is no direct experimental evidence that exercise is consistently terminated at a T_C of 40°C (Ely et al. 2009). In fact, the findings that the maximum T_C at exhaustion is dependent upon aerobic fitness level (Cheung and McLellan 1998; Selkirk and McLellan 2001) demonstrates the plasticity of this apparent hyperthermic threshold, and certainly indicates that the critical T_C upon which exercise is terminated is modified by the physiological parameters of a given individual. Likewise, the maximal tolerable T_C is likely influenced by a multitude of other factors which range from the magnitude of elevations in skin temperature and the narrowing of the core-to-skin temperature gradient (Cheuvront et al. 2010) to various psychological and perceptual inputs (Cheung 2007a, b, 2010b).

As the term suggests, an elevated T_C is a pre-requisite for hyperthermia induced exhaustion. However, hyperthermia elicits a cascade of physiological responses which range from an altered muscle metabolism (Mundel 2008), increased cardiovascular strain (Rowell 1974), a modification of neuromuscular (Cheung 2008) and cerebral (Nielsen and Nybo 2003) activity, and endotoxemia (Lambert 2008). Taken together, it is unlikely that a specific threshold T_C dictates exercise exhaustion in the heat, rather exhaustion is probably mediated by the combined stress placed on the physiological systems maintaining homeostasis (Gonzalez-Alonso et al. 2008b).

Notably, self-paced exercise performance is also attenuated by heat stress, which is likely similarly mediated by elevations in body temperatures (Abbiss et al. 2010; Altareki et al. 2009; Ely et al. 2010; Ely et al. 2009; Periard et al. 2011a; Tatterson et al. 2000; Tucker et al. 2004). However, at present, the elements dictating these voluntary reductions in exercise intensity remain largely undefined. Nevertheless, these will be specifically discussed later in this chapter (*see* 2.5.5: Behavioral Control of Exercise Intensity). The following will specifically address the apparent mechanisms and hypotheses associated with fixed-intensity exercise intolerance under heat stress. However, it is acknowledged that many (if not all) of these factors are likely involved whether exercise intensity is constant or variable.

Cardiovascular Challenges:

Based on observations that maximal heart rate is unaffected by atropine, a cardiac accelerator (Robinson et al. 1953), and that voluntary exhaustion in the heat occurs concomitant with the attainment of maximal heart rate (Craig and Froehlic 1968; Gonzalez-Alonso et al. 1999), attenuated exercise tolerance in the heat has historically been considered to be driven by cardiovascular factors – namely the availability of cardiac output to supply the working muscles (Rowell 1974). Accordingly, prolonged moderate intensity exercise in the heat elicits a significant cardiovascular challenge that is characterized by reductions in stroke volume, central blood volume, aortic pressure and cardiac output, and the attainment of near maximal heart rates (Rowell et al. 1966). Thus the suggestion that “...the greatest stress ever imposed on the human cardiovascular

system (except for severe hemorrhage) is the combination of exercise and hyperthermia (Rowell 1986)” seems justified. This statement is perhaps best exemplified in the acceleration of the inability of the cardiovascular system to maintain blood pressure during maximal exercise in the heat (Gonzalez-Alonso and Calbet 2003). Albeit indirectly, these data support the hypothesis that blood flow to the working muscles is limited by the reduced availability of cardiac output driven by increases in skin perfusion (Rowell 1974).

As described previously (*see* Figure 2.9), skin blood flow is markedly lower during exercise in the heat, relative to similar, passively induced, increases in body temperature (Johnson 1992; Kenney and Johnson 1992). In accordance, skin blood flow during upright exercise reaches a plateau at a T_C of $\sim 38^\circ\text{C}$ despite further increases in body temperatures (Bregelmann et al. 1977; Gonzalez-Alonso et al. 1999). Presumably, this response helps control arterial blood pressure which, although is usually slightly lower during exercise in the heat (Trinity et al. 2010), is generally well controlled when hydration (Gonzalez-Alonso et al. 1997) is preserved (Nielsen et al. 1997; Rowell 1974). Likewise, to the detriment of temperature regulation, this skin blood flow attenuation apparently helps maintain exercising muscle blood flow, which has been found to be unchanged during prolonged moderate intensity exercise undertaken in both hot and more moderate conditions (Nielsen et al. 1993; Nielsen et al. 1990; Nielsen et al. 1997; Savard et al. 1988). Notably however, muscle blood flow can become compromised with significant dehydration, but this is predominantly a function of a reduced perfusion pressure rather than a decrease in vascular conductance (Gonzalez-Alonso et al. 1998). Nevertheless, decreased muscle blood flow during dehydration does not affect aerobic metabolism, as this is maintained by an increase in O_2 extraction (i.e. widening of the arteriovenous O_2 difference) (Gonzalez-Alonso et al. 1998).

It appears that during prolonged exercise in the heat, skin blood flow is compromised, ensuring blood flow to the working musculature, suggesting that the reduced exercise capacity in the heat is not an outcome of an increased cardiovascular strain, (Crandall and Gonzalez-Alonso 2010; Gonzalez-Alonso et al. 2008a). However, the role of

cardiovascular strain in reducing exercise tolerance in the heat cannot be dismissed entirely. For instance, simultaneous with the progressive rise in T_C , heart rate increases and stroke volume decreases as a function of exercise duration, a process known as cardiovascular drift (Coyle and Gonzalez-Alonso 2001). In most circumstances cardiac output is well maintained (Ekelund 1967). However during prolonged exercise in the heat cardiac output is reduced (Rowell et al. 1966) likely as a function of heart rate approaching 'maximal' levels (Thompson 2006). In these instances, arterial blood pressure is reduced (Rowell et al. 1966), such that muscle perfusion pressure may be compromised, decreasing muscle blood flow (e.g. Gonzalez-Alonso and Calbet 2003; Gonzalez-Alonso et al. 1998). Although this remains very much an untested hypothesis, the observation that previously heat-exhausted subjects can resume exercise despite similarly elevated T_C by simply decreasing \bar{T}_{sk} (Dill et al. 1932), and presumably skin blood flow, has been proposed to support a cardiovascular limitation to exercise capacity in the heat (Rowell 1974). However, this apparent support is extremely questionable considering the cascade of physiological and perceptual responses that are elicited by skin cooling.

A different, yet related, hypothesis has been recently proposed explaining the observed decrements in exercise performance in the heat (Cheuvront et al. 2010). This hypothesis is predicated on the cardiovascular mediated (Gonzalez-Alonso and Calbet 2003) attenuation of $\dot{V}O_{2peak}$ in the heat (*see* 2.5.3.1: Maximal Oxygen Uptake). Additionally, under such circumstances, any given exercise intensity would elicit a higher percentage of $\dot{V}O_{2peak}$ ($\% \dot{V}O_{2peak}$), and as both $\dot{V}O_{2peak}$ and $\% \dot{V}O_{2peak}$ are potential factors dictating the performance of prolonged exercise (Bassett and Howley 2000; di Prampero 2003), sustainable exercise intensity, and therefore exercise duration, may be reduced in the heat via these factors (Cheuvront et al. 2010; Periard et al. 2011a). Although support for this hypothesis is mounting (Ely et al. 2010; Ely et al. 2009; Kenefick et al. 2010; Periard et al. 2011a), experimental testing is in its infancy and further research is required. Nevertheless, a more complete discussion of this hypothesis is presented later in the chapter (*see* Skin Temperature as a Controller of Exercise Intensity).

Further evidence of a role for the cardiovascular system to impact exercise tolerance and exertional heat illness may be derived from the re-distribution of blood flow associated with whole body heat stress during both rest and exercise. In accordance, decreased splanchnic blood flow may compromise the intestinal barrier, increasing permeability, and initiate a cascade of events perhaps mediating the development of exertional heat stroke (Lambert 2004, 2008). Likewise, it has been proposed that these factors may also contribute to the relative exercise intolerance in the heat (Cheung and Sleivert 2004b). While these hypotheses remain largely untested (Cheung and Sleivert 2004b; Lambert 2008), given their relevance to this thesis, their etiology are briefly addressed in the following paragraphs.

Under normal circumstances the intestinal barrier prevents the passage of potentially dangerous substances from within the intestinal lumen to the internal environment. However, if the integrity of this barrier becomes compromised, lipopolysaccharides (i.e. endotoxins) leak into the internal environment (Lambert 2008). Increased permeability is likely multi-factorial (Lambert 2004), but appears to be directly associated with ischemia induced (Hall et al. 1999) hypoxia (Unno et al. 1996), acidosis (Salzman et al. 1994) and hyperthermia (Dokladny et al. 2006; Lambert et al. 2002; Moseley et al. 1994). Hyperthermia alone also increases nitric oxide production in the splanchnic region, a substance known to further increase intestinal permeability (Hall et al. 1994). Given these conditions, intestinal hyperpermeability and the presence of endotoxins within the internal environment (i.e. endotoxemia) appear to be a common occurrence during prolonged intense exercise (Brock-Utne et al. 1988; Jeukendrup et al. 2000; Pals et al. 1997; Selkirk et al. 2008). Acutely, endotoxemia triggers cytokine release (Bouchama et al. 1991; van Deventer et al. 1990), perhaps promoting further heat storage (Sakurada and Hales 1998). This may be further confounded whereby during hyperthermia the nitric oxide production within the splanchnic region promotes splanchnic vasodilation (Hall et al. 2001), likely mediating profound hypotension, a characteristic of heat stroke (Kregel et al. 1988).

At present, the direct involvement of cytokines in the etiology of heat stroke is unclear (Leon 2006). Nevertheless, exertional heat stroke does appear to be tightly associated with the incidence of endotoxemia (Bouchama et al. 1991), while the inhibition of endotoxemia appears to decrease the risk of heat stroke (Gathiram et al. 1987). The involvement of endotoxemia in heat stroke remains very much a hypothesis. However, since intestinal hyperpermeability and the corresponding gastrointestinal symptoms appear prior to serious complications, it is possible that they may serve as a warning sign of a more severe condition if left unattended (Lambert 2008). This concept alone makes this an extremely valuable line of research, whereby the development of exertional heat stroke may be prevented.

Even less clear is that of the potential role of endotoxemia in exercise intolerance under heat stress. This hypothesis (Cheung and Sleivert 2004b) is based on the evidence for cytokines influencing exercise capacity at the level of the CNS (Davis and Bailey 1997). At present there is no such evidence for endotoxemia-induced cytokine production mediating exercise capacity in the heat. Interestingly however, relative to trained subjects, the cascade of endotoxemia-induced responses occurs at lower body temperatures in aerobically unfit individuals (Sakurada and Hales 1998; Selkirk et al. 2008), perhaps providing some explanation for the increased exercise capacity (Cheung and McLellan 1998; Selkirk and McLellan 2001) and improved tolerance of high T_{CS} (Cheung and McLellan 1998; Morrison et al. 2006; Selkirk and McLellan 2001) that accompanies greater aerobic fitness. Furthermore, an anecdotal relationship between dehydration, a perfusion pressure induced reduction in muscle blood flow (Gonzalez-Alonso et al. 1998), and gastrointestinal hyperpermeability (Lambert et al. 2008) is intriguing. However, it is unlikely that endotoxemia-induced hypotension (Kregel et al. 1988) plays a role in accelerating exercise exhaustion in the heat as the observed decline in arterial pressure occurs at T_C well above those typically observed at exhaustion in similar animals ($\sim 44^\circ\text{C}$ vs. $\sim 41^\circ\text{C}$) (Fuller et al. 1998; Walters et al. 2000). Nevertheless, it represents an interesting parallel that certainly warrants investigation.

Provided adequate hydration is ensured, the current body of literature indicates a relatively small direct role for the cardiovascular system limiting exercise duration in the heat. Notably however, the resolution of relatively untested hypotheses would strengthen this assertion. Nevertheless, as the increase in skin blood flow during exercise in the heat is often not sufficient to achieve heat balance, T_C rises to levels capable of impairing the ability to continue exercising (*see* 2.5.3.2: Heat Exhaustion) (Johnson 2010). Therefore, at present, it is clear that the cardiovascular system plays an indirect role in mediating the attenuation in exercise tolerance in the heat.

Muscle Metabolism and Function:

Moderate increases in body, specifically muscle, temperatures is thought to benefit metabolic processes by increasing the rate of all chemical reactions, enhancing nerve conduction and inducing conformational changes within the muscle. This dependency of chemical reaction speed on temperature is termed the Q_{10} effect, whereby an increase in muscle temperature by 10°C doubles the chemical and enzymatic reaction rate. Accordingly, increases in muscle temperature have been found to be beneficial for cycle sprint performance (Asmussen and Boje 1945; Linnane et al. 2004). However, that heat stress accelerates exhaustion implies that the Q_{10} effect may not be beneficial during pronounced hyperthermia. In fact, alterations in muscle function and metabolism may contribute to the attenuation in exercise duration observed in the heat (Febbraio 2000).

Exhaustion during prolonged moderate intensity exercise generally coincides with significant glycogen depletion (i.e. <150 mmol/kg dry weight) (Febbraio 2000). Therefore, when Fink et al. (1975) demonstrated a reduced reliance upon muscle triglycerides, an increased rate of muscle glycogen usage and higher lactate concentrations during exercise in the heat, these findings, in addition to other corroborating observations (Febbraio et al. 1994a; Febbraio et al. 1994b; Kozlowski et al. 1985), were hypothesized to contribute to the premature termination of exercise in the heat (Fink et al. 1975). As exercising muscle blood flow is unaffected by heat stress, (Nielsen et al. 1993; Nielsen et al. 1990; Nielsen et al. 1997; Savard et al. 1988) this increased glycogenolysis is unlikely associated with muscle ischemia, but rather it is

probably a direct consequence of elevated body temperatures (Febbraio 2000). Indeed, blunting the rise in body temperatures (both T_C and muscle temperature) during exercise, via both heat acclimation (Febbraio et al. 1994a) and exercise in the cold (Febbraio et al. 1996) reduced the reliance on muscle glycogen. These findings were taken a step further when it was demonstrated that the increased rate of glycogenolysis was specifically dependent on elevations in muscle temperature (Starkie et al. 1999). Accordingly, one may consider this enhanced glycogen depletion during exercise in the heat making a significant contribution to the accentuation in exhaustion. To the contrary however, exhaustion in the heat, relative to cooler conditions, is not associated with glycogen depletion (Figure 2.18B) (Parkin et al. 1999), indicating that the reduced exercise duration was related to processes other than carbohydrate availability (Febbraio 2000; Hargreaves 2008; Mundel 2008). This conclusion is indirectly supported by evidence suggesting the improvement in exercise performance by carbohydrate supplementation in the heat, is not mediated via alterations in substrate metabolism, but rather its apparent effects on the CNS (Carter et al. 2003).

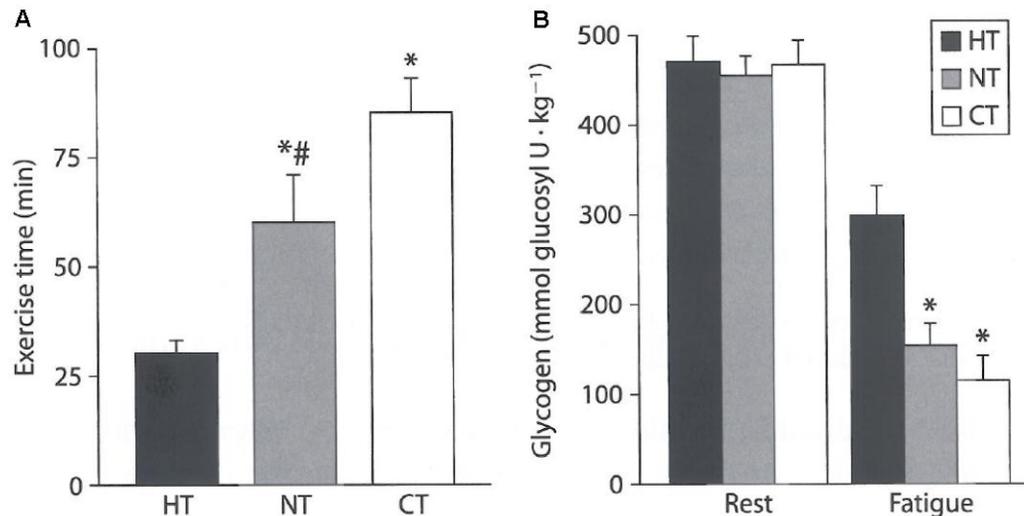


Figure 2.18: Exercise time-to-exhaustion (A) and muscle glycogen before (Rest) and after (Fatigue) prolonged exhaustive exercise (B) in 40°C (HT), 20°C (NT) and 3°C (CT). * indicates different from HT ($P < 0.05$); # indicates different from CT ($P < 0.05$) (Parkin et al. 1999).

Likewise, the contractile function of skeletal muscle is not likely affected by elevations in temperature. In accordance, brief maximal voluntary isometric (Nielsen et al. 1993; Nybo and Nielsen 2001a; Todd et al. 2005) and dynamic (Martin et al. 2005) muscle force production following prolonged exhaustive exercise is unchanged with hyperthermia, while single sprint performance is similarly unaffected (Drust et al. 2005). By contrast, sustained isometric (Ftaiti et al. 2001; Nielsen et al. 1993; Nybo and Nielsen 2001a; Todd et al. 2005) and prolonged dynamic (Martin et al. 2005) muscle force production is impaired with hyperthermia, which appears to be specific to the exercised muscle group (Saboisky et al. 2003). Likewise repeated sprint ability is reduced with elevations in T_C and muscle temperatures (Drust et al. 2005). These findings could be explained by *in vitro* data demonstrating that high muscle temperatures ($>43^\circ\text{C}$) compromised the function of the inner mitochondrial membrane, thereby reducing the adenosine diphosphate (ADP) to O_2 ratio and altering mitochondrial respiration (Brooks et al. 1971; Willis and Jackman 1994). However, this appears unlikely as the fatigability of intact skeletal muscle fibers is unaffected by similarly high temperatures (Place et al. 2009). Rather, it appears more likely that hyperthermia exerts its influence via its effects on the CNS activation of skeletal muscle (Nybo 2008).

The Central Nervous System:

A discriminating factor dictating the diagnosis of potentially life threatening heat stroke from that of the less dangerous heat exhaustion, is the deterioration of CNS functioning (Armstrong et al. 2007; Binkley et al. 2002). Therefore, any direct involvement (or impairment) of the CNS during exhaustive exercise in the heat is perhaps not surprising. In accordance, brain activity, measured via changes in electroencephalogram (EEG) power spectrum, is exceptionally temperature sensitive, such that small alterations in brain temperature induce rather large changes in brain activity (Deboer 1998). Indeed, extreme hyperthermia ($T_C = \sim 41.8^\circ\text{C}$) reduces cortical activity in a dose dependent manner (Dubois et al. 1980), while also eliciting significant neuromuscular dysfunction (Dubois et al. 1981). Notably, the voluntary cessation of exercise is also accompanied by distinguishable alterations in EEG activity in cats (Angyan and Czopf 1998). Thus,

hyperthermia, exercise exhaustion and brain activity are intimately related, and may affect the capability of the CNS to activate skeletal muscle.

Alterations in frontal cortex activity during exhaustive exercise in the heat were first observed by Nielsen et al. (2001). Under this EEG paradigm, 'alertness' – defined as a shift from high frequency β waves to low frequency α waves, i.e. an increase in the α/β wave ratio (Kandel and Schwartz 1985) – decreased over time through exhaustion in the heat. Notably, this ratio was unaffected by non-exhaustive exercise of similar duration in a more moderate environment (Nielsen et al. 2001). Using the same exercise protocol, these findings were confirmed a short time later (Nybo and Nielsen 2001c), whereby the EEG activity of the central and occipital cortices changed similar to that of the frontal cortex. Furthermore, the observed changes in EEG activity were found to be linearly related to the increase in the perception of exercise effort (Nybo and Nielsen 2001c), an established factor dictating the onset of exercise exhaustion (Enoka and Stuart 1992).

The abovementioned studies both compared brain activity during exhaustive, hyperthermic, exercise to that during non-exhaustive, normothermic, exercise (Nielsen et al. 2001; Nybo and Nielsen 2001c). While fatiguing exercise has been found to alter brain activity in cats (Angyan and Czopf 1998), it is entirely possible the EEG changes observed were driven by the exhaustive nature of the exercise, rather than hyperthermia. Indeed, Ftaiti et al. (2010) have recently demonstrated that the α/β wave ratio does in fact increase in both exhaustive normothermic and hyperthermic conditions. However, the rise in the α/β wave ratio is greater during exercise in the heat (Figure 2.19), even despite the shorter exercise duration. Thus, brain activity is substantially altered by both exhaustive exercise and hyperthermia.

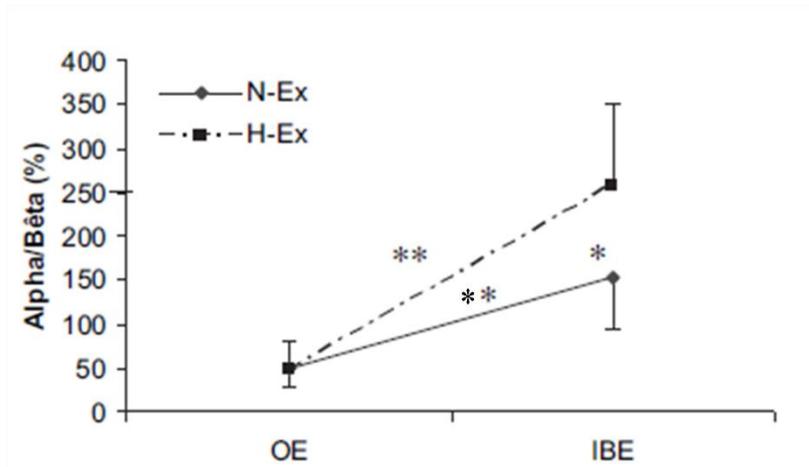


Figure 2.19: α/β wave ratio at the onset of exercise (OE) and immediately before exhaustion (IBE) during prolonged exhaustive exercise in both moderate (N-Ex) and hot (H-Ex) conditions. * denotes significant difference between sessions ($P < 0.05$); ** denotes significant increase over time ($P < 0.05$) (Ftaïti et al. 2010).

In explanation of their findings, Nybo and Nielsen (2001c) hypothesized that the changes in EEG activity and increases in the perception of effort observed during exhaustive exercise in the heat were elicited by a reduction in cerebral perfusion, hastening exhaustion. This hypothesis seems plausible since, just as occurs elsewhere in the body, during exercise in the heat the brain is in competition for the available cardiac output. Consequently, relative to exercise in a more moderate thermal environment, Nybo et al. (2001b; 2002b) identified reductions in middle cerebral artery mean blood velocity during exhaustive exercise in the heat. Although, this reduction could be partially explained by hyperthermia-induced hyperventilation (White 2006) and the subsequent decrease in the partial pressure of arterial CO_2 (Jorgensen 1995), this did not appear to be the sole determinant of this attenuation (Nybo and Nielsen 2001b). Since middle cerebral artery mean blood velocity may not always reflect changes in actual cerebral blood flow (Poulin et al. 1999), these findings were a short time later corroborated when global cerebral blood flow, as measured via the Kety-Schmidt technique – commonly regarded as the ‘gold’ standard method, was found to decline over time during exercise in uncompensable heat. No change over time was observed during exercise under more

moderate conditions (Nybo et al. 2002a; Nybo et al. 2002b). In this investigation however, the observed reduction in the partial pressure of arterial CO₂ was able to account for this reduction in cerebral blood flow (Nybo et al. 2002a). More recent evidence however, suggests that that this may only account for a portion of the observed reductions in cerebral blood flow occurring concomitant with hyperthermia (Brothers et al. 2009).

Reductions in cerebral perfusion during exercise are capable of limiting exercise duration should the metabolic demands of the brain not be met (Nybo and Rasmussen 2007). Thus, the pronounced regional increases in metabolism occurring during hyperthermia (Nunneley et al. 2002) must be adequately countered by decreasing the metabolic activity of other cerebral areas or the global cerebral metabolism will increase. Although the metabolic rate of a number of cerebral regions decreases during passive heating (Nunneley et al. 2002), the global cerebral metabolism does in fact increase during exercise in the heat (Nybo et al. 2001), and as can be inferred from above, this increased metabolism does not appear to require an increase in blood flow. Rather, an increase in O₂ and glucose extraction adequately maintains aerobic cerebral metabolism (Nybo et al. 2001). Thus, cerebral perfusion does not appear to limit the cerebral metabolism. Likewise, changes in mean middle cerebral artery blood velocity do not explain the observed changes in EEG activity or account for the increased perception of effort or exhaustion during exercise in the heat (Rasmussen et al. 2004). Hence, it appears that changes within the brain are a result of hyperthermia and are not simply the product of changes in another physiological variable (i.e. cerebral perfusion).

Although, alterations in arousal or the level of alertness quantified via changes in EEG activity cannot be explained by the changes in cerebral blood flow during exhaustive exercise in heat (Rasmussen et al. 2004), changes in the concentration of brain neurotransmitters may explain centrally mediated reductions in exercise capacity (Meeusen and Demeirleir 1995; Meeusen et al. 2006). Brain neurotransmitters - particularly increases in serotonin, reductions in dopamine or an increase in the serotonin/dopamine ratio (Davis and Bailey 1997), induce such states as lethargy and

drowsiness, and have been hypothesized to influence exercise capacity via these effects (Blomstrand et al. 1988; Davis and Bailey 1997; Newsholme 1986). It is out of the scope of this chapter to thoroughly review the general concept of central fatigue and brain neurotransmission. Therefore, please refer to Meeusen et al. (2006) for an in depth review. Nevertheless, given the cerebral alterations (Nybo et al. 2002a; Nybo and Nielsen 2001c), that the blood brain barrier may be compromised by exercise-induced hyperthermia (Watson et al. 2005b) and the role of neurotransmitters in temperature regulation (Lee et al. 1985), changes in brain neurotransmission may play a particularly large role in reducing exercise capacity in the heat (Meeusen and Roelands 2010; Roelands and Meeusen 2010). Indeed, blood prolactin levels, an indirect measure of the serotonin/dopamine ratio (Bridge et al. 2003b), are elevated by increases in body temperatures (Brisson et al. 1991), more specifically \bar{T}_{sk} (Bridge et al. 2003a; Mundel et al. 2006a), which increase progressively throughout exercise in the heat (Mundel et al. 2007).

Given the complexity of brain functioning and that the direct measurement of brain neurotransmitters in humans is not possible, experimental findings concerning the role of brain neurotransmitters in exercise capacity in the heat have generally been mixed (Maughan et al. 2007; Meeusen and Roelands 2010). In accordance, pharmacological serotonin reuptake inhibition (i.e. effectively increasing serotonin concentrations) does not appear to affect exercise capacity in the heat (Roelands et al. 2009; Strachan et al. 2004, 2005). By contrast however, acute dopamine reuptake inhibition (i.e. increasing dopamine concentrations) improves the performance of exercise in the heat (Bridge et al. 2003b; Roelands et al. 2008). These results are supported by the findings of Watson et al. (2005a) who, likely via bupropion derived dopamine reuptake inhibition (Roelands and Meeusen 2010), also observed an increase in exercise performance in the heat.

From this brief overview, it is clear that neurotransmission can modulate exercise capacity in the heat (Meeusen and Roelands 2010). Interestingly, this does not appear to be related to increases in serotonin (Roelands and Meeusen 2010). Nevertheless, perhaps most notable are the thermal (i.e. T_C) outcomes observed concurrent with improvements

in exercise performance in the heat associated with dopamine reuptake inhibition. For example, although the thermal stress was perceived as being no different, T_C was higher during the final stages of the self-paced exercise trial (Roelands et al. 2008; Watson et al. 2005a). Since exercise intensity was higher in this trial, this was likely a direct effect of the increased metabolic heat production. However, the signals indicating that the exerciser should reduce their exercise intensity – as observed in the placebo trials - were seemingly ignored (Roelands et al. 2008; Watson et al. 2005a) suggests that in situations where dopamine reuptake was inhibited, subjects were at an increased risk for heat illness (Meeusen and Roelands 2010).

Given their role within the CNS neurotransmitters within the brain are likely associated with altered cerebral activity. However, any connections between serotonin, dopamine and the abovementioned changes in EEG activity remain circumstantial. Notably however, the role of the CNS in exercise capacity in the heat cannot be limited to cerebral changes (Racinais and Oksa 2010). For instance, EEG changes with extreme hyperthermia (Dubois et al. 1980) coincide with significant neuronal dysfunction as measured via somatosensory evoked potentials from the finger (Dubois et al. 1981). Likewise, changes in motor cortical excitability (Todd et al. 2005), prefrontal cortex oxygenation (Morrison et al. 2009) or decreases in cerebral blood flow (Rasmussen et al. 2004) cannot explain attenuations in muscular performance during hyperthermia.

Despite the progressive development of hyperthermia, neuromuscular activity, as measured via electromyography (EMG), is unchanged throughout constant speed running in the heat (Ftaiti et al. 2001) and is similar during fixed-intensity bouts of cycling in both hot and moderate thermal conditions (Hunter et al. 2002). By contrast however, EMG activity, and thus skeletal muscle recruitment, is lower in the heat during prolonged self-paced cycling exercise compared to that in a cooler environment (Abbiss et al. 2010; Kay et al. 2001; Tucker et al. 2006; Tucker et al. 2004). However, as exercise intensity decreased in parallel with EMG activity in all instances, it is unclear as to whether neuromuscular skeletal muscle recruitment decreased exercise intensity or was a consequence of this intensity reduction.

Similar findings have been observed immediately following prolonged exercise in the heat. In accordance, EMG activity of the previously exercised muscle group has been demonstrated to reflect that of changes in prolonged muscle force production, which is reduced following exercise in the heat (Ftaiti et al. 2001; Martin et al. 2005; Nybo and Nielsen 2001a). These findings are not unanimous however, as Saboisky et al. (2003) and Abbiss et al. (2008) found force production and power output to be attenuated despite maintenance of EMG activity. Perhaps most interesting, is that in all of the abovementioned studies the observed reductions in voluntary force production were mostly due to reductions in voluntary (central) activation and not the inability of the muscle itself to produce an equivalent force output (Abbiss et al. 2008; Martin et al. 2005; Nybo and Nielsen 2001a; Saboisky et al. 2003). However, given that exercise undertaken in both hot and cool conditions has been shown to elicit similar post-exercise decrements in maximal force production and voluntary activation (Periard et al. 2011b), as presented, the contribution of hyperthermia alone remains unclear.

As extensively reviewed previously (*see* 2.5.3.2: Heat Exhaustion), increases in T_C have exclusively been hypothesized to mediate reductions in exercise tolerance in the heat. Therefore, an understanding of the effect of increases in body temperatures, in the absence of exercise, dehydration, cardiovascular strain, etc., on voluntary force production and the ability to voluntarily recruit skeletal muscle (i.e. voluntary activation) is advantageous. Although passive hyperthermia has limited effect upon dynamic (Cheung and Sleivert 2004a) and short duration (Nybo and Nielsen 2001a) maximal force production, it is nearly unanimously accepted that sustained voluntary force production is negatively influenced by increases in body temperatures (Morrison et al. 2004; Morrison et al. 2006; Morrison et al. 2009; Racinais et al. 2008; Thomas et al. 2006; Thornley et al. 2003; Todd et al. 2005). Similar to that observed following exercise induced hyperthermia, this force reduction is dictated primarily by a reduction in voluntary activation (Morrison et al. 2004; Morrison et al. 2006; Morrison et al. 2009; Thomas et al. 2006) occurring at or above the level of the motor cortex (Todd et al. 2005). However, the extent of decrease in force production may be partially mediated by changes at the spinal and sarcolemmal levels (Racinais et al. 2008). The extent of

decrease in voluntary force production and activation depends primarily on the extent of increase in T_C (Figure 2.20) (Morrison et al. 2004; Thomas et al. 2006) and appears to occur independent of regional changes in \bar{T}_{Sk} (Morrison et al. 2004; Racinais et al. 2008), thermal sensation and discomfort (Morrison et al. 2004), muscle temperature (Thomas et al. 2006), aerobic fitness (Morrison et al. 2006) or prefrontal cortex oxygenation (Morrison et al. 2009).

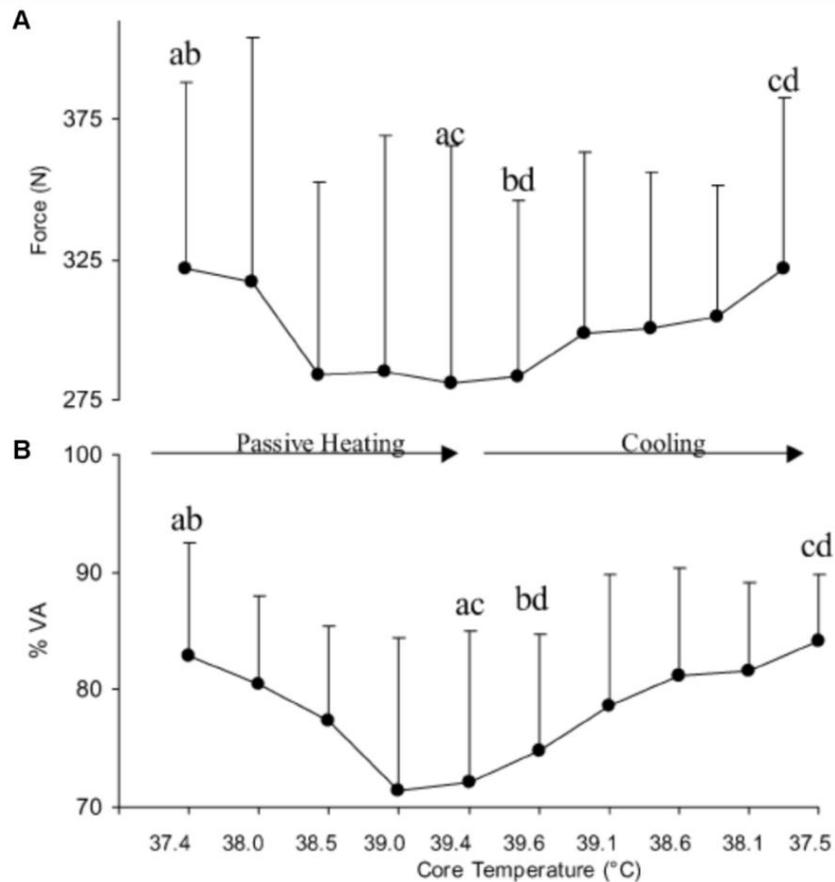


Figure 2.20: Knee extension maximal isometric force production (A) and voluntary activation (VA; B) during passive heating and cooling. Matching letters indicate significant differences ($P < 0.001$) (Morrison et al. 2004).

At present, it remains to be determined as to whether the observed changes in CNS functioning - from the level of the brain through to the innervation of skeletal muscle - associated with hyperthermia represent a failure or a regulated response (Racinais and Oksa 2010). For instance, the CNS seemingly protects the respiratory muscles during exhaustive exercise by cortically modulating neural drive (Verin et al. 2004), and a similar mechanism has been proposed with regards for exercise in the heat (Marino 2004). However, this theory of protective modulation by the CNS is confounded by the potentially modulatory factors occurring upstream of the motor cortex (Racinais and Oksa 2010), i.e. motivation, will, etc., that can significantly affect muscular performance (Bruck and Olschewski 1987). Nevertheless, according to the heat illness continuum this would appear an advantageous response. For instance, whether consciously or sub-consciously mediated, it can be reasonably inferred that reductions in the voluntary activation of skeletal muscle appear to terminate exercise prior to catastrophic hyperthermia, the loss of thermoregulation and the diagnosis of exertional heat stroke.

2.5.4: Considerations

It is unanimous that fixed-intensity exercise duration is attenuated in the heat relative to that in cooler, more moderate, environments. The mechanisms underlying this reduced exercise capacity are less clear, and likely involve changes in a variety of physiological processes ranging from the cardiovascular system through to the CNS. As the decision to cease exercise, i.e. exhaustion, is one of consciousness, it is likely that the ultimate mediator of this exercise intolerance resides within the CNS, more specifically, the brain. However, a multitude of factors associated with hyperthermia contribute to this decision. Investigations into the manner in which these various elements are integrated in order to reduce exercise duration is certainly warranted. Notably however, evidence for or against many of the hypotheses described above will undoubtedly resolve many of these issues.

Although briefly introduced, to this point, instances during which the exerciser controls the intensity of exercise (i.e. self-paced exercise) has been largely ignored. Although the physiological processes mentioned above likely play a role in dictating the selection of exercise intensity, hyperthermia is not commonly observed during these self-paced

situations. Thus, this behavior appears to prevent substantial hyperthermia and it is likely that the behavioral control of exercise intensity is dictated slightly differently than that incurring heat exhaustion. The sections that follow directly address the behavioral modulation of exercise intensity, its role in body temperature regulation during exercise and how these responses are controlled.

2.5.5: Behavioral Control of Exercise Intensity

In the previous discussion (*see* 2.4.4: Thermoregulatory Behavior), thermal behavior has been predominantly limited to voluntarily adjusting the external thermal environment, i.e. \bar{T}_{Sk} (Figure 2.14). However, behavioral responses can be similarly elicited by directly changing the internal thermal environment (i.e. T_C) (Cabanac 1996a). One example may be that of microwave exposure, whereby T_C can be directly behaviorally regulated independent of \bar{T}_{Sk} (Bruce-Wolfe and Adair 1985). Another, more relevant to this thesis, is the heat sink occurring subsequent to the consumption of cold beverages before or during exercise in the heat, e.g. Kay and Marino (2000). Accordingly, forced consumption of cold fluids pre- and during exercise reduces T_C , lengthening fixed-intensity exercise duration (Siegel et al. 2010) and improving self-paced exercise performance (Burdon et al. 2010; Stanley et al. 2010) in the heat. Furthermore, voluntary fluid intake is highest during fixed-intensity exercise in the heat when drink temperatures are cold, which reduces T_C and improves exercise duration (Mundel et al. 2006b). Thus, under this experimental paradigm voluntarily drinking cold beverages is a thermoregulatory behavior (Cabanac 1996a).

Another more common manner in which internal temperature can be behaviorally regulated is via voluntary muscular work, i.e. by controlling metabolic heat production (Cabanac 1996a). Thus, a notable example of thermoregulatory behavior is voluntary exercise (Mercer 2001). Anecdotally, this is probably with reference to voluntarily exercising in the cold to warm oneself. Indeed, experimental evidence indicates that spontaneous running activity in rodents increases as ambient temperature decreases (Fregly 1956; Gordon and Heath 1980). Although the precise nature of this behavior is

unknown, voluntary wheel running can be modulated by warming the T_{aHYP} , suggesting this response is, at least partially, thermal in nature (Gordon and Heath 1980).

Similar experimental evidence has been presented in humans. For instance, during cold exposure increases in voluntarily controlled exercise intensity have been found to appropriately attain thermal comfort, preventing a discernable drop in T_C (Cabanac and Leblanc 1983; Caputa and Cabanac 1980). Likewise, this selection of exercise intensity decreases as ambient temperature increases (Cabanac and Leblanc 1983) (Figure 2.21). Notably, as a drop in T_C does not appear a pre-requisite for initiating this behavior (Cabanac and Leblanc 1983; Caputa and Cabanac 1980), this situation reflects that of the control of thermal behavior during rest, where \bar{T}_{Sk} provokes behavior thereby regulating T_C (see 2.4.4: Thermoregulatory Behavior).

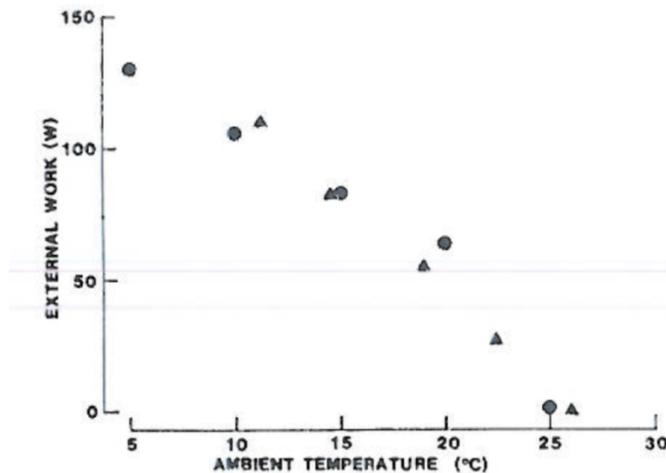


Figure 2.21: Intensity of exercise produced by one subject at the end of one hour of walking on a treadmill. The intensity of exercise chosen by the subject was proportional to ambient temperature, i.e. “was a clear cut thermoregulatory behavior.” (Cabanac and Leblanc 1983).

Although such relationships between voluntary exercise and ambient temperature are perhaps not unexpected, there may be instances where exercise must be undertaken despite elevations in ambient temperature. It is in these instances where the dissipation

of metabolic heat challenges regulation (*see* 2.5: Dynamic Exercise in the Heat). Thus, although not universally accepted as such, self-paced exercise under thermal stress may valuably contribute to our understanding of the control of thermoregulatory behavior (Flouris 2010). By utilizing our knowledge concerning the control of thermal behavior during instances of both rest and exercise in the cold, this section aims to (re-)evaluate the current body of literature concerning the voluntary control of exercise intensity under heat stress. It is hoped that what follows will make a valuable contribution to furthering our understanding of the control of human thermoregulatory behavior. This discussion may also bring to light further mechanisms underlying the impairment of self-paced exercise performance in the heat.

2.5.5.1: An Objective Definition of Thermal Behavior

Given that the voluntary control of metabolic heat production is not always accepted as a thermal behavioral response in the heat, it is advantageous to objectively define thermoregulatory behavior. In accordance, thermal behavior is any coordinated movement establishing a preferred condition for heat exchange between an organism and its environment (Mercer 2001). In the study of thermal physiology, this behavior is restricted to those actions elicited by a (central) nervous system (Mercer 2001). Ultimately, thermoregulatory behavior appears to achieve, and maintain heat balance, thereby suitably regulating T_C (Romanovsky 2007; Schlader et al. 2009). Furthermore, thermal behavior, as with most homeostatic behaviors (Cabanac 1992), appears to be initiated by a given level of negative affect (e.g. thermal discomfort and/or unpleasantness) (Cabanac 1971; Satinoff 1996). Finally, Cabanac (1996a) implicitly stated that in order for a behavior to be thermoregulatory in nature it must fulfill at least one of the following: 1.) The response must be accompanied by a symmetrical response, i.e. if it occurs in the heat it must not occur in the cold; 2.) The response must be a quantitative function of ambient temperature and/or body temperatures; and 3.) The response magnitude must be a function of the stimulus intensity. Where relevant, the following discussion of the literature will adhere to these thermal behavioral guidelines.

2.5.5.2: Metabolic Heat Production and Heat Stress

As would be expected, locomotor activity and metabolic heat production are decreased during and following heat exposure in rats (Shido et al. 1994; Shido et al. 1991). Similar evidence in humans can be found within the field of occupational physiology. For instance, the intensity of physical work has been observed to decrease with increases in ambient temperature (Gun and Budd 1995). Furthermore, during exposure to thermally stressful environments self-paced physical work is encouraged (Brake and Bates 2002b), which directly reduces the incidence of heat illness (Brake and Bates 2000, 2002a), a significant occurrence in many thermally stressful occupational environments (Donoghue et al. 2000), e.g. mining, etc. Additionally, self-paced work, defined as the rate of physical work (Brotherhood et al. 1997) or changes in the frequency and duration of informal rests and light activities (Budd et al. 1997c), substantially contributes to the regulation of T_C during fire suppression work under heat stress (Budd et al. 1997b). The impact of this behavior is considerable given that, in these instances, endogenous heat production constituted almost three quarters of the thermal load (Budd et al. 1997a). Thus, observations in occupational situations involving physical work bring to light the benefits of self-pacing and support the voluntary control of exercise intensity as a thermoregulatory behavior.

In the laboratory setting such connections between metabolic heat production and heat stress have been identified based on the principle that metabolic heat production rises with the mass of an individual and the intensity at which they are exercising (Nielsen 1996). These results however, are confounded by the experimental exercise protocol (or modality) utilized (Tucker 2008). For example, during fixed-intensity exercise in the heat, metabolic heat production is constant and heat dissipation is limited to autonomic responses. Thus, in an uncompensably hot environment, T_C rises, triggering a cascade of physiological responses, facilitating heat exhaustion (*see* 2.5.3.2: Heat Exhaustion). In contrast, when exercise is self-paced in similar conditions metabolic heat production can be controlled by the exerciser via adjustments in exercise intensity. Thus, when comparing exercise modalities, fixed-intensity exercise provides an all-or-none

behavioral response (i.e. exercise continuance or cessation), while self-paced exercise may provide insights into the initiation and control of this behavior (Flouris 2010).

As mentioned above (*see* 2.5.3: Ambient Temperature and Exercise Performance), non-laboratory based self-paced exercise performance is attenuated in the heat, indicating that voluntarily selected exercise intensity is also lower (Ely et al. 2007a; Ely et al. 2007b; Ely et al. 2008; Vihma 2010; Wegelin and Hoffman 2011). Given the apparent insights from occupational situations and the relationships between metabolic heat production, body mass and exercise intensity (Nielsen 1996), this is perhaps not unexpected. In accordance, this voluntary control of metabolic heat production has been experimentally verified. For instance, during marathon running in the heat, maximal running speed was found to be inversely proportional to body mass (Dennis and Noakes 1999), while the magnitude of reductions in exercise intensity in the heat are similarly proportionate (Marino et al. 2000). Likewise, during self-paced running in the heat, larger runners employ a slower self-selected running velocity than their smaller counterparts, despite similar performance characteristics (e.g. $\dot{V}O_2\text{max}$) and T_C and \bar{T}_{SK} (Marino et al. 2004). Altogether, these results indirectly indicate that during relatively prolonged self-paced exercise in the heat, the rate of metabolic heat production is a controlled variable.

Analogous findings are apparent when voluntarily selected exercise intensity responses are observed in a more homogenous subject population. In moderate thermal conditions, self-selected exercise intensity during prolonged (>2 min) duration exercise is maintained relatively constant over time (Abbiss and Laursen 2008), and is often characterized by a sharp increase in intensity during the final stages, i.e. an end-spurt (Catalano 1973, 1974). By contrast, Tatterson et al. (2000) observed that exercise intensity in the heat was reduced after completion of ~30% of a 30 min self-paced exercise task, which were confirmed a short time later by Tucker et al. (2004) during a similar self-paced bout of exercise. In both instances, T_C increased equally, independent of whether exercise was undertaken in a hot or a cooler environment. Notably, an end-spurt was also apparent (Tatterson et al. 2000; Tucker et al. 2004). Comparable results have been found during longer duration (≥ 60 min) self-paced exercise tasks, whereby exercise intensity is

voluntarily decreased during the early stages of exercise in the heat (Abbiss et al. 2010; Periard et al. 2011a). However in this paradigm, T_{CS} were elevated relative to the cooler conditions. Interestingly, in both studies there was evidence for the attainment of heat balance (Abbiss et al. 2010; Periard et al. 2011a). These results are similarly reflected by that of even shorter duration (<15 min) self-paced exercise, where, despite the equally occurring modest hyperthermia, exercise intensity is voluntarily reduced in the heat relative to cooler conditions (Altareki et al. 2009; Ely et al. 2010). Thus, high ambient temperatures are associated with reductions in exercise intensity. As exercise intensity (and body mass) is directly related to metabolic heat production, these studies certainly suggest that endogenous heat is being controlled in order to prevent a limiting rise in T_C and perhaps achieve heat balance.

Although within occupational physiology this behavior would be considered thermoregulatory in nature (e.g. Budd 2001), as presented, these studies are usually not considered as such, with papers stating otherwise comprising the minority (e.g. Maughan et al. 2007). Thus, the results of these studies lend themselves to the question, are voluntary reductions in exercise intensity in the heat thermal behaviors? According to the pre-established definition (*see* 2.5.5.1: An Objective Definition of Thermal Behavior) there is certainly some evidence that this may be the case. For instance, as exercise intensity only slightly varies over time in cooler, more moderate, thermal environments (Abbiss et al. 2010; Altareki et al. 2009; Ely et al. 2010; Periard et al. 2011a; Tattersson et al. 2000; Tucker et al. 2004), there is clear evidence that these responses occur only when exposed to a hot environment. Thus, they are quantitatively a function of the ambient environment and, presumably, physiological need, an important factor dictating the nature of this response (Cabanac 1996a). Furthermore, given that exercise itself is mediated by the CNS (Brooks et al. 2005) and that reductions in exercise intensity are characterized by decreases in EMG activity (Abbiss et al. 2010; Kay et al. 2001; Tucker et al. 2004), voluntary reductions in exercise intensity are elicited by a (central) nervous system. Likewise, there is some evidence that reductions in exercise intensity act to control the rise in T_C (Marino et al. 2004; Marino et al. 2000; Tattersson et al. 2000; Tucker et al. 2004), thereby achieving heat balance (Abbiss et al. 2010; Periard et al.

2011a), while finally, where reported, self-paced exercise in the heat is unanimously perceived as warm (Abbiss et al. 2010; Altareki et al. 2009; Periard et al. 2011a) and thermally uncomfortable (Periard et al. 2011a).

Although it does indeed appear that voluntary reductions in intensity during self-paced exercise in the heat are thermoregulatory behaviors, the present interpretation of these data is certainly not conclusive. For instance, these studies are simply observational and a study has not been undertaken in which these responses have been experimentally evaluated and identified as thermal behaviors. Furthermore, the precise role of behavior, independent from that of the concurrently active autonomic responses, on the thermal outcomes remains uncertain. For example, heat balance can be attained autonomically throughout a range of ambient temperatures (5°C - 30°C) (Nielsen and Nielsen 1962). Therefore, at present, there is no evidence that the rise in T_C and/or the attainment of heat balance is predominantly attributed to this behavior. Likewise, calorimetric estimates of heat losses and gains during self-paced exercise in the heat are also warranted. Thus, any modulation of the rate of metabolic heat production could be quantified.

It is certainly noteworthy that the behavioral control of exercise intensity appears to allow for successful completion of a given exercise task, without incurring heat exhaustion (Cheung 2007a; Tucker 2008). Thus, catastrophic hyperthermia and the development of heat illness are avoided (Marino 2004). This arrangement is supported in that self-pacing in hot occupational settings controls heat gain while reducing the incidence of heat illness (Brake and Bates 2000, 2002a). The same is likely true during exercise in the heat. For instance, in much the same way as the proposed heat illness continuum (*see* 2.5.2: Exertional Heat Illnesses), a thermoregulatory continuum may be similarly observed. For example, behavior appears to be preferentially elicited (i.e. self-paced exercise), however during instances where behavior is restricted (i.e. fixed-intensity exercise), when the signaling inputs to behave are ignored or when behavior is inadequate, heat exhaustion ensues. It is only upon the failure of both behavior and exhaustion that temperature regulation may be lost, homeostasis compromised, and exertional heat stroke becomes imminent (Figure 2.22).

This hypothesis is supported by the high incidence of exertional heat stroke when high motivation and external factors (e.g. a drill sergeant, coach, fellow runners, etc.) dictate exercise intensity (Armstrong et al. 2007; Donoghue et al. 2000; Epstein et al. 1999; Shibolet et al. 1976) and a lower incidence when people exercise alone or self-pace (Brake and Bates 2000, 2002a). Furthermore, this behavioral arrangement is similar to that of the thermoregulatory system at rest (*see* 2.4.4: Thermoregulatory Behavior), such that, during rest behavior is preferentially initiated by changes in \bar{T}_{sk} , thereby preventing changes in T_C . It is only when behavior is restricted or insufficient that T_C rises and autonomic thermoregulatory responses are elicited. In the circumstance that both behavioral and autonomic temperature regulation are inadequate, T_C will rise/fall uncontrollably, and temperature regulation may be lost. Thus, this paradigm compliments that of the heat illness continuum, and represents an intriguing hypothesis by which temperature regulation is maintained and heat illness is avoided in the heat, i.e. the ‘safety-brake’ (Cheung 2007a; Cheung and Flouris 2009). Moreover, given that the behavioral control of exercise intensity appears to modulate body temperature regulation, this provides further, albeit indirect, evidence for these exercise intensity responses to be considered thermal behaviors.

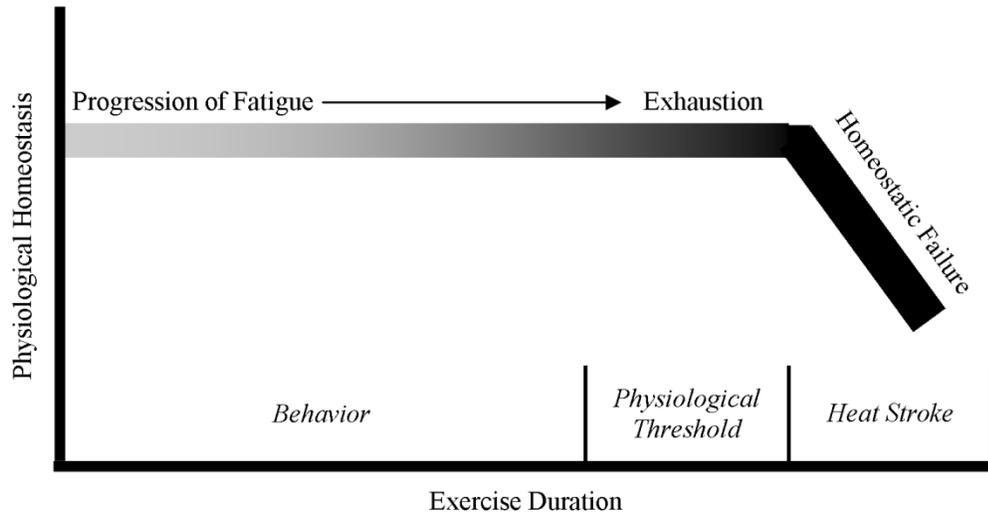


Figure 2.22: The thermoregulatory continuum hypothesis. Physiological homeostasis during exercise in the heat is maintained by (thermoregulatory) behavior and a (multi-system) physiological threshold that dictates heat exhaustion. Temperature regulation is maintained until exercise is continued after the attainment of heat exhaustion, beyond which physiological homeostasis is compromised and the development of exertional heat stroke most likely ensues.

2.5.5.3: *The Voluntary Control of Exercise Intensity*

How metabolic heat production is controlled has little effect on whether voluntary adjustments in exercise intensity in the heat are thermal behaviors. Thus, to this point, this section has largely ignored those factors potentially involved in the control of exercise intensity in the heat. Nevertheless, an appreciation of the control of these responses would certainly enhance our understanding of thermoregulatory behavior during instances of both rest and exercise (Flouris 2010), which, considering our relatively limited understanding of the control of this thermo-effector (see 2.4.4: Thermoregulatory Behavior), is perhaps the most enduring issue.

The physiological and perceptual factors dictating the voluntary control of exercise intensity in the heat is a topic of considerable discussion (e.g. Cheung 2010b; Chevront et al. 2010; Crewe et al. 2008; Marcora 2007; Marcora 2008; Noakes et al. 2005; Tucker

2009; Tucker et al. 2007b; Tucker and Noakes 2009). Although great strides have been made, much remains uncertain. For instance, paramount to this debate is whether these responses are consciously or subconsciously mediated (Flouris 2010; Maughan 2010). As it pertains to thermoregulatory behavior, this would be important as quantitative investigations into the control of human thermal behavior typically define it in terms of a conscious response (e.g. Flouris and Cheung 2008; Schlader et al. 2009). Predominantly based on the evidence suggesting that the ideal selection of exercise intensity during competition is, at least in part, a learned response (e.g. Mauger et al. 2009; Micklewright et al. 2010)), Maughan (2010) contends this is a consciously mediated process. Still, others insist these responses are subconsciously mediated (Noakes et al. 2005; St Clair Gibson and Noakes 2004; Tucker et al. 2004). Notably, this debate does not directly provide insights into the physiological mechanisms dictating these responses. Thus, at this point, whichever hypothesis prevails may prove to be irrelevant.

The signals mediating behavioral temperature regulation during exercise are likely different than those at rest (Bleichert et al. 1973). In accordance, the *combination* of both autonomic (eccrine sweating) and behavioral (exercise intensity) responses regulates T_C during competitive tennis undertaken in a moderately warm environment (Morante and Brotherhood 2008). Thus, a given level of sweating is likely a requirement for thermal comfort (Fanger 1970). Therefore, any apparent relationships between autonomic and behavioral temperature regulation at rest, do not appear to apply during exercise (Havenith et al. 2002). However, the controlling factors dictating exercise intensity responses in the heat appear remarkably similar to those initiating thermal behavior during rest (*see* 2.4.4: Thermoregulatory Behavior), as they are likely to be dictated by perception as mediated by physiological responses associated with changes in body temperatures.

Perceptual Control of Exercise Intensity:

Thermal discomfort has been suggested to decrease work and athletic performance (Vanos et al. 2010). Anecdotally, this is probably due to its influence on the motivation to continue exercising in a hot environment (Cotter et al. 2001). However, the precise

role of thermal discomfort in the decision to continue or cease exercising (or to adjust exercise intensity) remains uncertain. This is likely explained by distinct changes in the meaning of 'comfort' occurring with exercise (Havenith et al. 2002). For example, despite profuse sweating and the redistribution of blood, an exercising individual is prepared and expectant of being uncomfortable (Cabanac 2006b; Parsons 2003), while sensations of pleasure, productivity, and achievement may also be associated with physical and thermal strain (Ekkekakis 2003; Havenith et al. 2002). Alternatively, current evidence indicates that the perception of effort may be the ultimate modulator of exercise intensity (Brotherhood et al. 1997; Johnson et al. 2009; Joseph et al. 2008; Tucker 2009; Ulmer 1996) and during instances of heat stress thermal discomfort may play a more modulatory role (Marcora 2007).

By definition, the rating of perceived effort (or exertion) (RPE) is intended to integrate signals of both central (e.g. cardio-respiratory, CNS, etc.) and peripheral (e.g. muscles, joints, etc.) in origin into a single indicator of perceived strain, which is measured on a subjective scale, e.g. the Borg RPE scale (Borg 1982). Regardless of ambient conditions, neural activation of skeletal muscle raises the RPE in a dose-dependent manner (Noble and Robertson 1996), but no single physiological variable consistently explains the RPE (Hampson et al. 2001). However, depending on the circumstances, a specific physiological cue may take precedence and become the predominant mediator of the RPE (Pandolf 1982). Notably, physiological factors only account for ~67% of the RPE variance, suggesting that the remaining variance is psychologically mediated (Morgan 1973).

Afferent feedback has been suggested to predominantly modulate RPE (Ulmer 1996). In contention, it has also been put forth that RPE is independent of this feedback, and instead is driven by efferent signals that are controlling down-stream physiological processes (Marcora 2009). At a given exercise intensity, perceived effort does not 'plateau' for 1 - 2 min, indicating during the transient from rest to exercise afferent feedback signals may be driving the RPE (Ulmer 1996). However, after this marked perceptual lag there is probably a balance between afferent and efferent mechanisms

(Noble and Robertson 1996), whereby afferent feedback modifies the efferent RPE signals (Hampson et al. 2001).

With direct regards to exercise in the heat, independent of differences in T_C , RPE is generally elevated at a given exercise intensity in the heat (Bergh et al. 1986; Maw et al. 1993; Pivarnik et al. 1988), suggesting that during such instances, factors associated with warm \bar{T}_{Sk} are dictating the RPE response (e.g. Pandolf 1982). However, should T_C be elevated, RPE in the heat appears to be predominantly a function of T_C (Nielsen and Nybo 2003; Nybo and Nielsen 2001c; Rasmussen et al. 2004). Interestingly, this arrangement mirrors that of the perceptual control of thermal behavior at rest where thermal discomfort is mediated predominantly by change in \bar{T}_{Sk} , unless there is a change in T_C , at which point T_C then becomes the primary dictator of discomfort (*see* 2.4.4.3: Thermal Modulation of Discomfort).

Consequently, the question now arises as to how RPE can control exercise intensity. Evidence may be found in the proposal that voluntary maximal force production may in fact be limited by a perceptual barrier, rather than one that is physiologically based *per se* (Banister 1979). Thus, decrements in prolonged maximal isometric (Ftaiti et al. 2001; Nielsen et al. 1993; Nybo and Nielsen 2001a; Todd et al. 2005) and dynamic (Martin et al. 2005) muscle force production and voluntary activation during hyperthermia could, in theory, be explained by the attainment of a maximal RPE at previously sub-maximal levels of force production. Notably, this has been suggested to limit findings indicating that the CNS is negatively affected by hyperthermia (Racinais and Oksa 2010) and is a process known to be associated with muscular fatigue (Enoka and Stuart 1992).

During exhaustive fixed-intensity exercise, RPE increases linearly over time in a manner proportionate to the *relative* trial duration (Eston et al. 2007; Horstman et al. 1979; Noakes 2004). Thus, the rate of rise in RPE early during exercise appears to adequately predict exercise duration (Horstman et al. 1979), a process known as teleoanticipation (Ulmer 1996). Indeed, this process may explain the observations of accelerated exhaustion in the heat. For instance, Crewe et al. (2008) identified that, compared to

cooler conditions, the premature cessation of fixed-intensity exercise in the heat was predicted by the increased rate of rise in RPE in the early stages of exercise. Notably, this enhanced RPE response occurred when T_{CS} were similar, suggesting this response was probably mediated by elevated \bar{T}_{sk} s (Crewe et al. 2008). Thus, as exhaustion in both hot and cooler environments is associated with the attainment of a near-maximal RPE (e.g. Galloway and Maughan 1997; Gonzalez-Alonso et al. 1999; Hunter et al. 2002; Saboisky et al. 2003), it is possible that the attenuated exercise duration in the heat can be explained by an increased rate of rise in the RPE. In these instances the combination of elevations in \bar{T}_{sk} and T_C , and the cascade of physiological and perceptual events that follow, or occur concurrently, undoubtedly play a major role in this RPE response.

In a way similar to that occurring during fixed-intensity exercise, during self-paced exercise the RPE rises relative to the proportion of the exercise task completed, with a near-maximal RPE being attained during the final stages of exercise (Albertus et al. 2005; Joseph et al. 2008). Furthermore, when expressed in proportion to the relative task length, this RPE response is well preserved and appears independent of (time) feedback (Albertus et al. 2005; Mauger et al. 2009) or ambient conditions, e.g. hypoxia/hyperoxia (Johnson et al. 2009; Joseph et al. 2008; Tucker et al. 2007a) or heat stress (Abbiss et al. 2010; Periard et al. 2011a; Tucker et al. 2004), amongst others. Thus, the exerciser appears to be comparing how they feel to how they expected themselves to feel at that moment in time and are adjusting their exercise intensity in order to protect this relationship (Joseph et al. 2008). Hence, changes in RPE may explain voluntary reductions in exercise intensity in the heat.

Indeed, by instructing subjects to adjust their exercise intensity in order to maintain an RPE between 'hard' and 'very hard' on the Borg 16 point scale (Borg 1970), Tucker et al. (2006) demonstrated that exercise intensity decreased over time until it could no longer continue at the required RPE. Perhaps most importantly, exercise duration, and thus the rate of decrease in exercise intensity, was shortest during exposure to hot ambient temperatures. Although it was concluded that the rate of heat storage mediated these reductions in exercise intensity (Tucker et al. 2006), the manner in which it was measured

appears to invalidate this conclusion (Jay and Kenny 2009). Rather, as exercise intensity became reduced at a point when T_{CS} were similar and \bar{T}_{SK} elevated, suggests that \bar{T}_{SK} mediated this response (Jay 2009). Further evidence for the role of RPE in controlling exercise intensity in the heat may be found when dopamine reuptake is inhibited (Meeusen and Roelands 2010). In such instances, self-paced exercise performance in the heat has been found to be improved, while the RPE response to this exercise remained similar. As a consequence however, T_C was found to be higher during the latter stages of exercise (Roelands et al. 2008; Watson et al. 2005a). Thus, dopamine reuptake inhibition appears to have altered the relationship between body temperatures and RPE, such that a higher exercise intensity was selected in order to maintain a similar RPE, but perhaps to the detriment of body temperature regulation.

Based on our current understanding of the control of exercise intensity during self-paced exercise, voluntary reductions in exercise intensity in the heat may be explained as follows. RPE is elevated at a given exercise intensity in the heat (Bergh et al. 1986; Maw et al. 1993; Pivarnik et al. 1988), while the rise in RPE is maintained independent of the ambient thermal environment (Abbiss et al. 2010; Periard et al. 2011a; Tucker et al. 2004). Thus, a reduction in exercise intensity must transpire. In order for this decrease in exercise intensity to occur there must be a reduction in voluntary neuromuscular activation (Abbiss et al. 2010; Kay et al. 2001; Tucker et al. 2004). If exercise is commenced at a normothermic T_C , these responses will be mediated predominantly via elevated \bar{T}_{SK} (Abbiss et al. 2010; Ely et al. 2010; Tatterson et al. 2000; Tucker et al. 2004). By contrast, if T_C is hyperthermic, T_C will likely dictate changes in exercise intensity (Altareki et al. 2009; Marino et al. 2004; Marino et al. 2000; Periard et al. 2011a). However, as changes in exercise intensity are mostly elicited prior to differences in T_C (Abbiss et al. 2010; Ely et al. 2010; Tatterson et al. 2000; Tucker et al. 2004) and appear to be a (thermal) behavior controlling the rise in T_C , preventing excessive hyperthermia and heat exhaustion (*see* 2.5.5.2: Metabolic Heat Production and Heat Stress), it appears that in most circumstances the RPE is likely dictated by increases in \bar{T}

T_{sk} . Thus, just as T_C is known to mediate exercise duration and performance, \bar{T}_{sk} is also a likely controller of exercise intensity.

Skin Temperature as a Controller of Exercise Intensity:

Voluntary exercise intensity responses do not appear to be associated with limiting alterations in metabolism (Periard et al. 2011a; Tatterson et al. 2000), while reductions in muscle blood flow also appear an unlikely influence (Nielsen et al. 1993; Nielsen et al. 1990; Nielsen et al. 1997; Savard et al. 1988). Although an argument can be made for a cardiovascular limitation (see below), it would seem these responses are predominantly related to elevations in body temperatures. In most situations changes in exercise intensity are elicited prior to differences in T_C (Abbiss et al. 2010; Ely et al. 2010; Tatterson et al. 2000; Tucker et al. 2004). Thus, there is some rather circumstantial evidence for elevations in \bar{T}_{sk} , and any associated physiological and perceptual consequences, as a controller of exercise intensity (Jay 2009; Marcora 2007).

To date, direct evidence for \bar{T}_{sk} as a controller of exercise intensity is extremely limited. For instance, Kay et al. (1999) observed that, in the absence of differences in T_C , self-paced exercise performance was improved when \bar{T}_{sk} was reduced upon exercise commencement, implying that selected exercise intensity was higher in this condition. Unfortunately, exercise intensity over time was not reported, while a role for T_C cannot be discounted as T_C was lower during the \bar{T}_{sk} cooling trial during the latter stages of exercise (Kay et al. 1999). Thus, the precise role of \bar{T}_{sk} currently remains unknown. Nevertheless, elevated \bar{T}_{sk} have been hypothesized to influence self-selected exercise intensity via its effects on the cardiovascular system (Cheuvront et al. 2010) and/or by stimulating changes in thermal perception (Marcora 2007).

As has been briefly introduced above (*see Cardiovascular Challenges*), the cardiovascular consequences associated with elevated \bar{T}_{sk} have been hypothesized to drive the observed voluntary reductions in exercise intensity in the heat (Ely et al. 2010; Ely et al. 2009;

Kenefick et al. 2010; Periard et al. 2011a). According to this hypothesis, reductions in peak cardiac output reduce MAP (Rowell et al. 1966) and consequently active muscle blood flow (Gonzalez-Alonso and Calbet 2003). In turn, $\dot{V}O_{2peak}$ is reduced (Arngrimsson et al. 2004; Arngrimsson et al. 2003; Pirnay et al. 1970; Wingo et al. 2005) and, as a consequence, any given exercise intensity would represent a higher percentage of $\dot{V}O_{2peak}$ ($\% \dot{V}O_{2peak}$), both of which are potential factors limiting the performance of prolonged exercise (Bassett and Howley 2000; di Prampero 2003). Notably however, it remains unclear as to whether a change in $\dot{V}O_{2peak}$ is a pre-requisite for alterations in $\% \dot{V}O_{2peak}$ and thus sustainable exercise intensity.

At present, experimental evidence for this hypothesis is rather circumstantial. Nevertheless, Kenefick et al. (2010) by observing the interactions between ambient temperature, hypohydration, and self-paced exercise performance interpreted their data in support of this hypothesis. In accordance, the negative impact of hypohydration on exercise performance was found to be strongly affected by increases in ambient temperature, which was likely mediated by an inability to maintain MAP, presumably an outcome of the competition for blood flow between the skin and muscle (Kenefick et al. 2010). Similarly, during prolonged self-paced exercise in the heat, increases in cardiovascular strain (i.e. increases in heart rate, and reductions in cardiac output, stroke volume and MAP) were found to be associated with reductions in exercise intensity and $\dot{V}O_{2peak}$, measured during the final stages of exercise (Periard et al. 2011a). However, in this paradigm, hyperthermia was clearly evident throughout most of the exercise bout in the heat (Periard et al. 2011a). Thus, these results may not explain reductions in exercise intensity prior to substantial increases in T_C (Abbiss et al. 2010; Ely et al. 2010; Tattersson et al. 2000; Tucker et al. 2004). Needless to say, despite a growing acceptance within thermal physiology (Ely et al. 2010; Ely et al. 2009; Kenefick et al. 2010; Periard et al. 2011a), this hypothesis remains essentially untested.

With considerations for exercise during hypoxia (or altitude) exposure, further indirect evidence for changes in $\dot{V}O_{2peak}$ dictating self-selected exercise intensity may become

apparent. In a linear dose-response manner, $\dot{V}O_{2peak}$ is reduced with increasing altitude (Wehrlein and Hallen 2006). Likewise, it is well established that sustained (>2 min) exercise performance deteriorates with altitude (Peronnet et al. 1991). Decrements in both exercise performance and $\dot{V}O_{2peak}$ at altitude are dictated by the inability to maintain arterial O_2 saturation (Chapman et al. 2010), which initiates a cascade of potentially limiting steps ranging from the level of the CNS (Amann et al. 2006) to oxygen delivery to the working muscle (Levine 2008). Thus, during prolonged exercise, reductions in $\dot{V}O_{2peak}$ appear to be related to reduced exercise performance, and therefore, the voluntary selection of a lower exercise intensity. However, whether a progressive and acute reduction in $\dot{V}O_{2peak}$, as occurs with increasing hyperthermia (e.g. Arngrimsson et al. 2004), can account for the observed reductions in exercise intensity remains uncertain. Still, one could interpret voluntary reductions in exercise intensity occurring shortly after the initiation of a hypoxic ‘challenge’ during self-paced exercise as being such evidence (Johnson et al. 2009). However, these findings should be transferred to instances of heat stress with caution as, for instance, hypoxia during exercise directly reduced arterial O_2 saturation (Johnson et al. 2009), a regulated physiological variable. By contrast, exercise intensity is commonly observed to be voluntarily reduced in the heat prior to differences in T_C (Abbiss et al. 2010; Ely et al. 2010; Tatterson et al. 2000; Tucker et al. 2004), and thus appear influenced by a controlling, but not a regulated, variable (i.e. \bar{T}_{sk}).

Given the apparent role for RPE mediating the selection of exercise intensity, further evidence for changes in $\dot{V}O_{2peak}$ mediating alterations in exercise intensity may be derived from the relationship between $\% \dot{V}O_{2peak}$ and RPE. For instance, $\% \dot{V}O_{2peak}$ appears to be an important RPE input (Berry et al. 1989; Pandolf et al. 1984) and is particularly relevant during instances of hypoxia exposure (Robertson 1982). Thus, alterations in $\dot{V}O_{2peak}$ may ultimately dictate exercise intensity via the $\% \dot{V}O_{2peak}$ elicited by a given exercise intensity and its subsequent influence on RPE. In contrast however, under thermal stress the relationship between RPE and $\% \dot{V}O_{2peak}$ is distorted (Pivarnik et al. 1988; Toner et al. 1986), suggesting that $\% \dot{V}O_{2peak}$ may not be a suitable

input for the selection of exercise intensity in the heat. Even still, there is little doubt that $\dot{V}O_{2peak}$ significantly impacts prolonged exercise performance (Bassett and Howley 2000; di Prampero 2003). Thus, the limited, albeit indirect, evidence for this hypothesis is rather intriguing. Nevertheless, at present the role of acute, progressive and rather small (during instances when only \bar{T}_{sk} is elevated) reductions in $\dot{V}O_{2peak}$ on self-selected reductions in exercise intensity in the heat remains uncertain.

Marcora (2007) has recently proposed that reductions in exercise intensity in the heat when exercising at a constant RPE (Tucker et al. 2006) are predominantly dictated by increases in \bar{T}_{sk} and the accompanying sensations of warmth and thermal discomfort. According to this hypothesis these thermal perceptual responses translated into elevations in RPE, thereby reducing exercise intensity (Marcora 2007). Given that there is some evidence that reductions in exercise intensity in the heat are thermoregulatory behaviors (*see* 2.5.5.2: Metabolic Heat Production and Heat Stress) and that this arrangement is extraordinarily similar to that of the control of thermal behavior at rest (*see* 2.4.4: Thermoregulatory Behavior), this hypothesis is certainly intriguing.

Indirect evidence for thermal perception as the ultimate modulator of RPE and exercise intensity may be found when comparing aerobically trained and untrained individuals. Accordingly, trained individuals consistently perceptually underestimated their physiological strain (a function of heart rate and T_C), while the untrained population appropriately perceived similar levels of physiological strain (Tikusis et al. 2002). Additionally, this perceptual difference was likely dictated by differences in thermal comfort, which was deemed more uncomfortable by the untrained group (Tikusis et al. 2002). Interestingly, in addition to many other factors, these findings may contribute to the increased exercise tolerance in the heat observed in trained populations (Cheung and McLellan 1998; Selkirk and McLellan 2001). By contrast however, there is evidence against this perceptually based arrangement, as prolonged maximal isometric force production has been found to be attenuated during hyperthermia despite improvements in thermal discomfort (Morrison et al. 2004). However, in this situation T_C was markedly elevated and was therefore likely dictating the maximal RPE response (Morrison et al.

2004). Nevertheless, to date there is no direct evidence for or against thermal perception as the ultimate modulator of exercise intensity in the heat.

Finally, it is notable that the apparently distinct hypotheses explaining reductions in exercise intensity in the heat (i.e. reduced $\dot{V}O_{2\text{peak}}$ and increased thermal discomfort) are not autonomous. Rather, it is more likely that they both contribute to the attenuation in self-paced exercise performance in the heat. For instance, given that $\dot{V}O_{2\text{peak}}$ is minimally affected when T_C is normothermic and only \bar{T}_{Sk} is elevated, it is most likely that thermal perception plays a large role in reducing exercise intensity during the initial stages of exercise. However, when T_C becomes substantially elevated and the deterioration of $\dot{V}O_{2\text{peak}}$ becomes more pronounced, reductions in $\dot{V}O_{2\text{peak}}$, and the accompanying increase $\% \dot{V}O_{2\text{peak}}$ at a given exercise intensity, likely plays a larger role. Although compelling, experimental support for this arrangement is required. Nevertheless, an integrative overview of the potential factors controlling exercise intensity in the heat is presented in Figure 2.23.

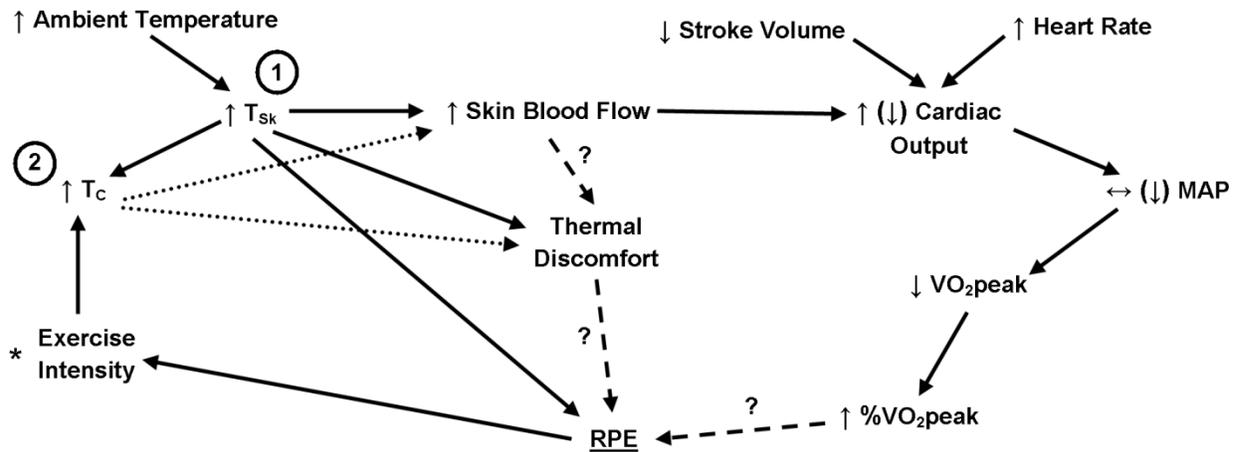


Figure 2.23: A hypothesized overview of the manner in which exercise intensity in the heat is controlled. The cascade of events begins with the initiation of exercise (denoted by: *), which combined with high (denoted by: ↑) ambient temperatures, and thus elevated \bar{T}_{sk} , increases core body temperature (T_c) due to an increased metabolic heat production. However, as exercise intensity can be reduced prior to differences in T_c , these responses are likely initially mediated by elevated \bar{T}_{sk} (1) either directly via its influence on perceived exertion (RPE) or indirectly via its influence on thermal discomfort or skin blood flow. In the heat, cardiac output is usually enhanced promoting blood flow to the skin while maintaining (denoted by: ↔) mean arterial pressure (MAP). However, with heat stress stroke volume falls (denoted by: ↓) as heart rate increases, and cardiac output can be compromised (i.e. reduced; denoted by: (↓)). In this instance, MAP may drop (denoted by: (↓)) thereby attenuating peak oxygen uptake ($\dot{V}O_{2peak}$). Thus, a given exercise intensity will elicit a higher percentage of $\dot{V}O_{2peak}$ ($\% \dot{V}O_{2peak}$), likely elevating RPE (hypothesis is denoted by: ? and dashed line). Likewise, thermal discomfort, either directly via the elevated \bar{T}_{sk} or indirectly via increases in skin blood flow (? , dashed line), may also independently elevate RPE at any given exercise intensity (? , dashed line). RPE is controlled independent of ambient temperature, and is thus, the controlling variable (denoted by underline) dictating changes in exercise intensity. Any factor raising or lowering RPE at a given exercise intensity will alter the selection of exercise intensity, thereby affecting the rate of metabolic heat production and therefore T_c . Should exercise intensity be held constant or if the drop in intensity is not sufficient and T_c continues to rise, elevated T_c likely dictates this cascade of events (2), perhaps via many of the same pathways (denoted by: dotted line).

2.5.5.4: *An Integrative View*

Recently, behavioral control during exercise has been a hotly contested topic (e.g. (Ekblom 2009a; Ekblom 2009b; Jay 2009; Jay and Kenny 2009; Marcora 2007; Marcora 2008; Marino et al. 2009; Noakes and Marino 2009a, b; Tucker et al. 2006, 2007b). The prominent model surrounding this controversy is that of the ‘central governor’ (Noakes 2011; Noakes et al. 2005; Noakes and St Clair Gibson 2004; St Clair Gibson and Noakes 2004). This model hypothesizes that exercise intensity is ultimately mediated by RPE via a ‘central governor’ with inputs predominantly dictated by motivational factors and afferent feedback (St Clair Gibson and Noakes 2004). Thus, this model is not fundamentally different than the paradigm presented previously (*see* 2.5.5.3: The Voluntary Control of Exercise Intensity). However, as it is well established that the control of exercise behavior is dictated by the brain and the CNS (Brooks et al. 2005), a strong argument can be made that there is no need to include a ‘central governor’ in this model (Levine 2008; Shephard 2009), as it may represent an ‘unnecessary’ step (Marcora 2008).

Given the role of behavior in physiology, i.e. that behavior aids the regulation of many physiological systems (and thus homeostasis) (Figure 1.1), the relevance of a particular model may actually be immaterial. For instance, external work, whatever its purpose, is a behavior (Cabanac 1987). Hence, voluntary alterations in exercise intensity are therefore, by definition, behaviors. In accordance, homeostatic behavior appears to be optimized by the affective sensations aroused by a given situation (Cabanac 1971). In this arrangement, the hedonic sensations elicited by homeostatic behaviors are hierarchally organized, such that the condition in which affective sensation is optimized is actively sought (Cabanac 1986, 1992, 2005, 2006b; Cabanac and Leblanc 1983; Johnson and Cabanac 1983).

The same appears to be true during exercise. In experimental circumstances, subjects voluntarily perform exercise to the best of their ability and are motivated to do so. Thus, they are prepared to encounter both a certain level of pain, displeasure, or discomfort (i.e. negative affect), and a given amount of pleasure (i.e. positive affect) (Cabanac 2006b;

Ekkekakis 2003). As negative affect is dictated by inputs of both central and peripheral origins (Cabanac 1986, 2006b), this is probably reflected in the predictable rise in RPE. However, should more discomfort be encountered than anticipated, an uncontrolled rise in RPE will follow. This arrangement is seemingly mirrored by that of the control of RPE, where a specific cue may take precedence and become the predominant mediator of the RPE response (Pandolf 1982). Notably, with regards for behaviors serving a homeostatic purpose, the origin of this hedonic sensation must mostly be physiological in nature (Cabanac 1971), which, again, is similar to that of the factors controlling RPE (Morgan 1973). Ultimately, this paradigm may explain both fixed-intensity and self-paced exercise outcomes under a wide array of circumstances, whereby any physiological factor known to modify the RPE at a given exercise intensity will, in some way, impact exercise performance or duration.

With direct regards for this thesis, reductions in exercise intensity during self-paced exercise in the heat appear to aid body temperature regulation (*see* 2.5.5.2: Metabolic Heat Production and Heat Stress). Thus, they can be considered homeostatic behaviors. Therefore, behavioral protection of RPE appears to adequately explain voluntary reductions in exercise intensity in the heat. In accordance, prior to changes in T_C , elevations in \bar{T}_{SK} elicit negative affect as mediated by changes in thermal discomfort and/or reductions in $\dot{V}O_{2peak}$ and the subsequent increase in $\% \dot{V}O_{2peak}$ at a given exercise intensity. In turn, at a given exercise intensity, RPE is therefore elevated. As changes in RPE over time are controlled, exercise intensity must be reduced (Figure 2.23). Under this paradigm, if T_C does become elevated, either via a constant intensity or an insufficient reduction in exercise intensity, this negative affect is likely driven by factors associated with T_C , as indirectly supported by the observations that T_C is capable of dictating the RPE response (*see* Perceptual Control of Exercise Intensity). Notably, the pathways by which T_C dictates exercise intensity may be similar to those elicited by \bar{T}_{SK} . However, as has been discussed above (*see* 2.5.3.2: Heat Exhaustion), this process may also include, amongst other changes, alterations in CNS functioning.

As a final point of discussion, the approach presented may be particularly useful as it is not limited to only exercise situations. It would seem highly implausible that during exercise the body would control behavior in a manner different than that occurring at rest. Rather, it would appear the process of interoception, i.e. feelings and sensations related to the physiological condition of the body (Craig 2002), would be processed similarly in both resting *and* exercising situations. The only apparent difference in the control of (thermal) behavior during exercise, compared to when at rest, probably lies within the concept of RPE (Figure 2.14A vs. Figure 2.24). Thus, a behavioral control model specific to exercise is not a requirement. Notably, this arrangement bears resemblance to that of psychobiological models proposed to explain various behaviors (Brehm and Self 1989; Ekkekakis 2003; Wright 1996). Indeed, some of these have recently been applied to exercising situations (Acevedo and Ekkekakis 2001; Ekkekakis 2003; Marcora 2008; Marcora and Staiano 2010; Marcora et al. 2009). Although it is out of the scope of this thesis to discuss, in depth, these psychological models dictating behavior, the control of homeostatic behavior undoubtedly lies within both the fields of *both* physiology and psychology (Cabanac 1996a, b; Cheung 2007b). This certainly represents an interesting corollary, warranting cross-disciplinary awareness and investigation.

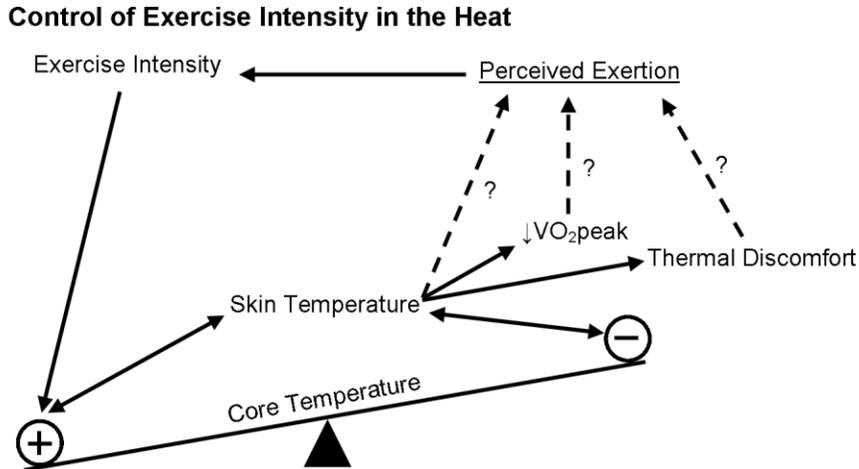


Figure 2.24: A simplified schematic demonstrating the control of exercise intensity during self-paced exercise in the heat. Heat gain (denoted by: +) is inevitable as metabolic heat production outweighs heat loss (denoted by: -) capabilities. However, elevations in skin temperature (\bar{T}_{sk}), either directly or indirectly via its influence on peak oxygen uptake ($\dot{V}O_{2peak}$) and thermal discomfort, increases perceived exertion (RPE). As RPE is the controlling variable (denoted by: underline), an increase in RPE initiates a voluntary reduction in exercise intensity, thereby restoring RPE. This reduction in exercise intensity decreases metabolic heat production (heat gain) helping to regulate body temperatures. Notably, this arrangement is remarkably similar to that of the control of thermoregulatory behavior at rest. Currently unknown pathways are denoted by a ? and a dashed line.

2.6: Perspectives

The purpose of this literature review was two-fold. The first objective was to establish guidelines that would be adhered to throughout the remainder of this thesis. This included a definition of the regulated variable (i.e. T_C), a general overview of the neurophysiological regulatory pathways and the manner in which this variable is regulated during instances of heat stress and/or exercise. Notably, the role of temperature regulation in behavior was emphasized as this is a focus of this thesis. The second objective was to critically review the literature concerning the manner in which exercise intolerance is mediated in the heat. This included an overview of the effects of heat stress on $\dot{V}O_2\text{max}$, exercise time-to-exhaustion and self-paced exercise performance both in the field and in the laboratory. Within this second objective it is obvious that there are numerous hypotheses that have yet to be experimentally tested, and evaluation of these hypotheses will undoubtedly improve our understanding of the factors reducing exercise capacity in the heat. An emphasis within this final objective was that of the voluntary control of intensity during self-paced exercise in the heat. Similarities between human thermoregulatory behavior during rest and that of the voluntary control of exercise intensity in the heat have become apparent. Thus, an understanding of the control of exercise intensity in the heat may provide valuable insights into the control of human thermoregulatory behavior on the whole. Conversely, applying our knowledge of control of human thermoregulatory behavior during rest to that during exercise may also help to further our understanding of the voluntary controls of exercise intensity under thermal stress. This integrative approach is the primary focus of this thesis.

CHAPTER THREE

3.0: Research Aims and Hypotheses

The experimental studies presented in the thesis were planned subsequent to the primary review of literature (*see Chapter Two*), which identified the short-comings and hypotheses in the rather broad research area. Although there were numerous research avenues established, the voluntary control of exercise intensity in the heat was chosen as the research topic of interest. As a result of the literature review, similarities between the control of thermoregulatory behavior during rest and the control of exercise intensity in the heat became apparent. The overall objective of this thesis was established accordingly.

The purpose of this thesis is to further the understanding of the control of human thermoregulatory behavior by using a self-paced exercise and exogenous heat stress model. In order to accomplish this objective, self-selected exercise intensity responses in the heat had to, first, be established as thermoregulatory behaviors (General Aim I). As presented previously, there is certainly evidence indicating this may be the case. However, formal testing of this hypothesis is warranted. Secondly, should the evidence from General Aim I indicate that voluntary reductions in exercise intensity in the heat are thermoregulatory behaviors, this self-paced exercise and heat stress model can then be used to directly test the hypotheses proposed to mediate reductions in exercise intensity in the heat (General Aim II). Ultimately, these findings could be applied to that of our more general understanding of the control of human thermal behavior.

3.1: Aims

General Aim I was first investigated by assessing the thermal and physiological outcomes of self-paced exercise in uncompensable heat relative to those occurring during fixed-intensity exercise in the same thermal environment (**Chapter Five**). This was considered valuable as, relative to when exercise intensity is constant, heat exhaustion is usually avoided when exercise is self-paced. Thus, the voluntary control of exercise intensity appears to modulate temperature regulation, suggesting that self-selected exercise intensity is a thermal behavior. This information may also

further our understanding of the manner in which exercise intolerance is mediated during instance of imposed intensity and/or adjustable intensity exercise, i.e. the thermoregulatory continuum hypothesis (Figure 2.22).

Subsequently, General Aim I was further addressed by comparing the self-selected exercise intensity responses occurring in the heat to those occurring in cooler environments (**Chapter Six**). Based on the pre-established definition of thermoregulatory behavior this investigation formally evaluated self-selected exercise intensity responses in the heat as thermal behaviors. Together with the observations from **Chapter Five**, these data will either support or refute the proposal that self-paced exercise in the heat can be used as a thermal behavioral model.

Given that the evidence from General Aim I ultimately suggested that reductions in exercise intensity in the heat are thermoregulatory behaviors (*see* **Chapter Five** and **Chapter Six**), the studies conducted towards General Aim II attempted to elucidate the control of this behavior. Specifically, \bar{T}_{sk} (**Chapter Seven**), thermal perception (**Chapter Eight**), and $\dot{V}O_{2peak}$ (**Chapter Nine**) were formally tested as potential modulators of exercise intensity in the heat. Notably, these studies comprising General Aim II, provide valuable data concerning not only the control of voluntary exercise intensity in the heat, but also provide insights into the control of thermal behavior in general. The results of these studies are discussed in this manner.

General Aims I and II can be split into more specific objectives. These are presented in the following.

General Aim I:

- 1.) Establish a formal relationship between fixed-intensity and self-paced exercise in the heat (**Chapter Five**).
- 2.) Investigate whether reductions in exercise intensity in the heat are thermoregulatory behaviors (**Chapter Six**).

General Aim II:

- 1.) Examine \bar{T}_{sk} as a controller of exercise intensity (**Chapter Seven** and **Chapter Eight**).
- 2.) Investigate the role of thermal perception on the voluntary selection of exercise intensity in the heat (**Chapter Eight**).
- 3.) Identify the role of $\dot{V}O_{2peak}$ as a determinant of exercise intensity in the heat (**Chapter Nine**).

3.1: Hypotheses

The review of literature (*see Chapter Two*) identified and generated numerous experimental hypotheses specific to those objectives described within both General Aims I and II. The specific hypotheses that were tested in the experimental studies of this thesis were as follows.

Specific Hypotheses:

- 1.) Exercise modality (i.e. fixed-intensity vs. self-paced) will modulate body temperature regulation when exposed to uncompensable heat stress (**Chapter Five**).
- 2.) Voluntary reductions in intensity during self-paced exercise in the heat are, by definition, thermoregulatory behaviors (**Chapter Six**).
- 3.) Voluntarily selected exercise intensity will be inversely related to \bar{T}_{sk} (**Chapter Seven**).
- 4.) Independent of changes in skin temperature, thermal perception (i.e. thermal discomfort and sensation) will modulate the voluntary selection of exercise intensity in the heat (**Chapter Eight**).
- 5.) Reductions in $\dot{V}O_{2peak}$ will be related to voluntary reductions in exercise intensity in the heat (**Chapter Nine**).
- 6.) During self-paced exercise, the rise in RPE will be maintained irrespective of differences in ambient (**Chapter Six** and **Chapter Nine**) or skin (**Chapter Seven**) temperatures.

CHAPTER FOUR

4.0: General Methodology

The purpose of this chapter is to describe the experimental methodology that was utilized throughout all of the subsequent experimental chapters. These methods were used in every experimental chapter. The recording intervals and additional procedures used within each individual study are outlined in the specific experimental chapter.

4.1: Pre-Experimental Trial Control

In all studies, all subjects were requested to arrive at the laboratory for the experimental trials having refrained from strenuous exercise, alcohol, caffeine, and tobacco for 24 h. To minimize variations in pre-exercise muscle glycogen content and hydration status, subjects were required to complete a 48 h diet and activity log before the first trial, and were instructed to follow the same diet and activities prior to each experimental trial. All subjects appeared to have complied with these requests. To maintain a hydrated state subjects drank a pre-measured bolus of water (5 ml/kg of body weight) 2 h prior to each experimental trial and adequate hydration was confirmed in all trials by a nude body weight within 200 g, core temperature within 0.2°C, and resting heart rate within six beats of the values in the previous trial (Montain and Coyle 1992).

4.2: Experimental Measurements

4.2.1: Anthropometric Characteristics

In all experimental trials, the subjects' height and weight were measured using a stadiometer (Seca, Bonn, Germany) and scale (Jandever, Taiwan), from which body surface area was estimated (Dubois and Dubois 1916). The scales were calibrated using standard weights. Seven site skinfold thickness was measured in triplicate using a Harpenden Skinfold Caliper (Baty International, UK) at the chest, axilla, triceps, subscapula, abdomen, suprailliac, and thigh. Percent body fat (Siri 1961) was estimated from body density (Jackson and Pollock 1978).

4.2.2: Heart Rate

Throughout all experimental trials heart rate was monitored and recorded from a heart rate monitor (Polar Vantage XL, New Zealand).

4.2.3: Mean Skin Temperature

In all experimental trials four calibrated surface thermistors (Grant Instruments Ltd., UK) were secured in place with Transpore™ Surgical Tape (3M Healthcare, USA) to the chest, thigh, leg, and arm on the right side of the body for determination of \bar{T}_{sk} according to the following equation: $\bar{T}_{sk} = 0.3 \cdot (\text{chest} + \text{arm}) + 0.2 \cdot (\text{thigh} + \text{leg})$ (Ramanathan 1964).

4.2.4: Ratings of Perceived Exertion

RPE was measured on the 15-grade (from 6 to 20) Borg rating of perceived exertion scale (Borg 1970), and was administered according to the recommendations set forth by Noble and Robertson (1996). In all experimental trials the subject's RPE was identified and recorded by the subjects placing a mark within box corresponding to their RPE (Figure 4.1). During any preliminary and/or familiarization sessions the subjects were fully acquainted with this scale prior to experimental use. This familiarization generally included defining perceived exertion, anchoring the perceptual range, explaining the nature and use of the scale, and answering the subject's questions (Noble and Robertson 1996).

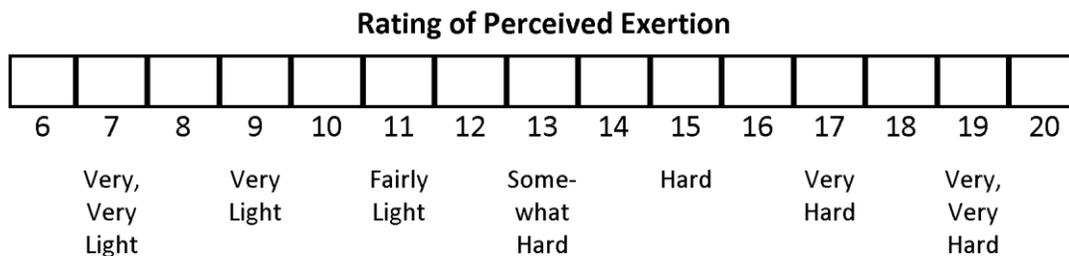


Figure 4.1: An example of the rating of perceived exertion (RPE) scale used in all experimental trials. The subject's RPE was identified and recorded by placing a mark in the appropriate box.

4.2.5: Thermal Sensation and Discomfort

Whole body (and regional, where necessary) thermal discomfort and thermal sensation were determined on four (from 1, comfortable, to 4, very uncomfortable) and seven (from 1, cold, to 7, hot) point scales, (Gagge et al. 1967). In all experimental trials the subject's thermal discomfort and thermal sensation were recorded by the subjects placing a vertical mark on the horizontal line (McIntyre 1980). The corresponding level of sensation and discomfort was measured at the location where these lines intersected. These scales were calibrated so that thermal discomfort and sensation were measured to the nearest 0.1. An example of these scales is presented in Figure 4.2. The subjects were fully familiarized with these scales prior to their experimental use. This familiarization included defining thermal discomfort ('How comfortable are you in this thermal condition?') and thermal sensation ('What temperature sensation do you feel right now?') (Parsons 2003), anchoring the perceptual range, and answering the subject's questions.

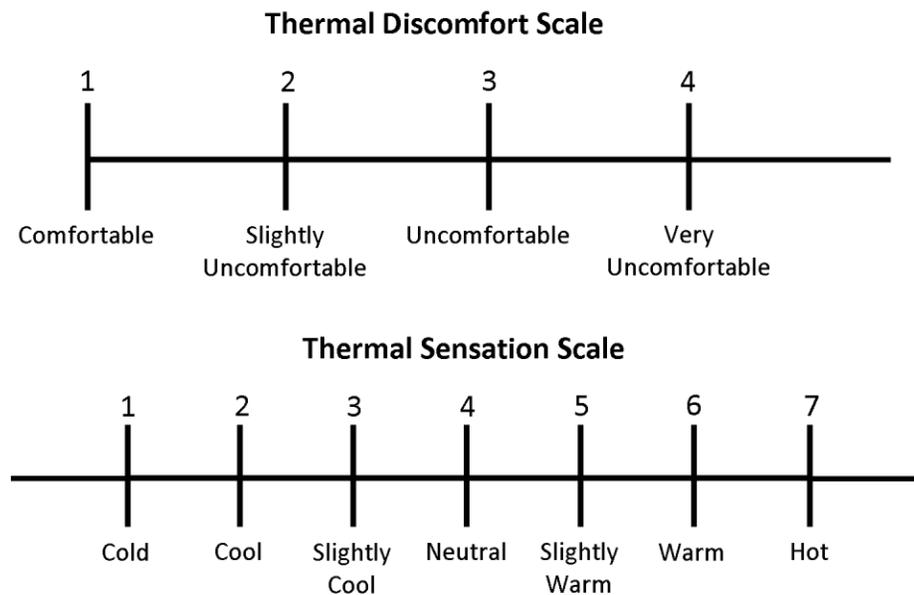


Figure 4.2: An example of the thermal discomfort and thermal sensation scales used in all experimental trials. The subject's thermal discomfort and thermal sensation were measured and recorded by the subjects placing a vertical mark on the horizontal line.

CHAPTER FIVE

5.0: Exercise Modality as a Modulator of Body Temperature

Regulation during Exercise under Uncompensable Heat Stress

Publication(s) based on this chapter:

Schlader ZJ, Stannard SR, Mundel T. (2011). Exercise and heat stress: Performance, fatigue and exhaustion – A hot topic. *Br J Sports Med* 45: 3-5

Schlader ZJ, Raman A, Morton RH, Stannard SR, Mundel T. (2011). Exercise modality modulates body temperature regulation during exercise under uncompensable heat stress. *Eur J Appl Physiol* 111: 757-766

Abstract

The purpose of this investigation was to evaluate exercise modality (i.e. self-paced or fixed intensity exercise) as a modulator of body temperature regulation under uncompensable heat stress. This was accomplished comparing the physiological outcomes of self-paced and fixed-intensity exercise in the heat. Eight well-trained male cyclists completed (work-matched) fixed-intensity (FI) and self-paced (SP) cycling exercise bouts in a hot (mean \pm SD; $40.6 \pm 0.2^{\circ}\text{C}$) and dry (relative humidity: $23 \pm 3\%$) environment estimated to elicit 70% of $\dot{V}\text{O}_2\text{max}$. Exercise intensity (power output) decreased over time in SP, which resulted in a longer ($P < 0.001$) exercise duration (FI: 20.3 ± 3.4 min, SP: 23.2 ± 4.1 min). According to the heat strain index, the modification of exercise intensity in SP improved ($P < 0.05$) the compensability of the thermal environment which, relative to FI, was likely a result of the reductions ($P < 0.05$) in metabolic heat production. Consequently, the rate of rise in core body temperature was higher ($P < 0.01$) in FI ($0.108 \pm 0.020^{\circ}\text{C}/\text{min}$) than in SP ($0.082 \pm 0.016^{\circ}\text{C}/\text{min}$). Interestingly, cardiac output, stroke volume, and heart rate during exercise were independent of exercise modality ($P > 0.05$). However, core body temperature (FI: $39.4 \pm 0.3^{\circ}\text{C}$, SP: $39.1 \pm 0.4^{\circ}\text{C}$), blood lactate (FI: 2.9 ± 0.8 mmol/L, SP: 2.3 ± 0.7 mmol/L), perceived exertion (FI: 18 ± 2 , SP: 16 ± 2), and physiological strain (FI: 9.1 ± 0.9 , SP: 8.3 ± 1.1) were all higher ($P < 0.05$) in FI compared to SP at exhaustion / completion. These data indicate that when exercise is self-paced, voluntary modification of metabolic heat

production improves the compensability of the thermal environment and reduces thermoregulatory strain. Therefore, under uncompensable heat stress, exercise modality modulates body temperature regulation.

Keywords

Exercise Intensity, Thermal Behavior, Thermal Compensability

5.1: Introduction

Body temperature is regulated via the control of autonomic and/or behavioral responses that modulate body heat exchange (Romanovsky 2007). According to the heat balance equation, when heat gain outweighs heat loss, body heat storage increases, elevating body temperatures. During fixed-intensity (constant power) exercise, metabolic heat production is constant, and therefore heat loss is limited solely to autonomic responses. Consequently, core body temperature rises until heat balance is achieved, as indicated by a 'plateau' in core temperature (Nielsen and Nielsen 1962; Saltin and Hermansen 1966).

During fixed-intensity exercise when exposed to uncompensable heat stress, by definition, the attainment of heat balance is impossible (Cheung et al. 2000) with core temperature rising linearly as a function of the metabolic and ambient heat loads (Robinson 1963) until exhaustion occurs (Cheung 2007a; Cheung and Sleivert 2004b). This inability to continue exercising in a hot environment, i.e. heat exhaustion (Armstrong et al. 2007), is directly associated with the failure to achieve heat balance, as heat exhaustion is accompanied by high core temperatures (Gonzalez-Alonso et al. 1999) and an increased challenge for the cardiovascular system to simultaneously meet the demands for both the working musculature and temperature regulation (Rowell 1974). Thus, thermal and cardiovascular regulatory processes have been included as important factors mediating the multi-system development of heat exhaustion (Armstrong et al. 2007; Cheung 2007a; Cheung and Sleivert 2004b; Gonzalez-Alonso et al. 2008a; Nybo 2008).

By contrast, during self-paced exercise in the heat the thermal compensability of the environment is likely improved by the exerciser by reducing exercise intensity, and thus metabolic heat production (i.e. exercise intensity; Tatterson et al. 2000; Tucker et al. 2004). This response has been suggested to occur primarily to control the rise in core body temperature (Marino 2004), but as a consequence exercise performance is reduced relative to more moderate conditions (Tatterson et al. 2000; Tucker et al. 2004). Notably, under self-paced conditions potentially critical levels of physiological stress are anticipated (Marino 2004) and therefore heat exhaustion is usually avoided (Brake and Bates 2002a).

To facilitate heat loss, autonomic responses are likely maximized as exercise progresses in uncompensable heat. Hence, fixed-intensity and self-paced exercise modalities (e.g. Tucker 2008) must modulate body temperature regulation differently. For example self-paced exercise seemingly utilizes behavior in order to improve the compensability of the thermal environment, while fixed-intensity exercise continues until an apparent (multi-system) physiological ‘threshold’ is reached and exercise can no longer be sustained (Cheung 2007a; Cheung and Sleivert 2004b; Nybo 2008). Thus, the two exercise modalities evaluate different physiological processes, and accordingly, the theories underlying the observed decrements in exercise performance/duration (Galloway and Maughan 1997; Parkin et al. 1999; Tatterson et al. 2000; Tucker et al. 2004) have been built up in opposition (Cheung 2007a; Tucker 2008). However, despite suggestions that future research should incorporate both modalities (Cheung 2007a; Cheung and Flouris 2009), an established relationship between the physiological outcomes obtained from both fixed-intensity and self-paced exercise remains elusive.

Given the dearth of evidence for a relationship between the physiological outcomes of fixed-intensity and self-paced exercise in the heat, a retrospective analysis of the previously published literature comparing the physiological and thermal outcomes of fixed-intensity and self-paced exercise in the heat was conducted as pilot work for this study. The methods for this analysis are presented in Appendix E. This analysis ultimately revealed that the level of physiological strain was lower upon completion of

self-paced exercise when compared to exhaustive fixed-intensity exercise in the heat (Table 5.1). The purpose and hypotheses for the subsequent formal investigation were established accordingly.

Table 5.1: A comparison of physiological strain upon completion of fixed-intensity and self-paced exercise in the heat.

Exercise Protocol	T _{Co}	T _{Ct}	HR _o	HR _t	PSI ¹
Fixed-Intensity					
70% VO ₂ max (Galloway & Maughan, 1997)	37.8	40.1	68	174.0	10.0
55 - 77% VO ₂ max (Nielsen <i>et al.</i> 1990)	36.4	39.3	70	183.3	9.2
60% VO ₂ max (Gonzalez-Alonso <i>et al.</i> 1999)	37.4	40.2	95	197.4	11.4
60% VO ₂ max (Nybo & Nielsen, 2001)	37.1	40.0	60	179.0	10.0
Mean		39.9*		183.4*	10.1*
Self-Paced					
20 km time-trial (Tucker <i>et al.</i> 2004)	37.5	39.2	60 ²	184.0	8.6
8 km run (Marino <i>et al.</i> 2004)	37.8	39.4	60 ²	187.5	8.9
8 km run (Marino <i>et al.</i> 2000)	37.0 ²	39.5	60 ²	186.0	9.4
30 min time-trial (Tatterson <i>et al.</i> 2000)	37.0 ²	39.2	60 ²	195.0	9.3
Mean		39.3		188.1	9.1

PSI, Physiologic Strain Index ¹ as calculated: $PSI = 5(T_{Ct} - T_{Co}) / (40.0 - T_{Co}) + 5(HR_t - HR_o) / (180 - HR_o)$ where: T_{Co}, mean resting core temperature (°C); T_{Ct}, mean core temperature at exhaustion/completion (°C); HR_o, mean resting heart rate (bpm); HR_t, mean heart rate at exhaustion/completion (bpm). ² T_{Co} and HR_o not provided, estimated as 37.0°C and 60 bpm. * Significantly different from self-paced exercise (P<0.05).

The purpose of this investigation was to evaluate exercise modality as a modulator of body temperature regulation, thus establishing a formal relationship between fixed-intensity (FI) and self-paced (SP) exercise in the heat. This was accomplished by testing the hypothesis that the freedom to behaviorally thermoregulate during SP exercise would increase exercise duration and improve the compensability of the thermal environment. Furthermore, it was also hypothesized that the magnitude of change in the cardiovascular and thermoregulatory responses would be lower during and upon completion of SP exercise relative to FI exercise to voluntary exhaustion.

5.2: Methods

5.2.1: *Experimental Overview*

Eight well-trained male cyclists completed FI and SP cycling exercise under uncompensable heat stress. During FI subjects rode until volitional exhaustion, while during SP the subjects completed the same amount of work as completed during FI, but exercise intensity (power output) was freely adjustable. All trials took place at the same time of day and there were 7 days between each trial.

5.2.2: *Subjects*

Eight healthy and well-trained male cyclists agreed to participate in the study. The subject's characteristics were (mean \pm SD): age, 34 ± 9 y; height, 1.8 ± 0.1 m; weight, 70.1 ± 6.2 kg; body surface area (BSA), 1.87 ± 0.11 m²; maximal oxygen uptake ($\dot{V}O_{2\max}$), 4.94 ± 0.41 l/min; and percent body fat, $10.6 \pm 3.3\%$. Each subject was fully informed of the experimental procedures and possible risks before giving informed, written, consent. The protocol was approved by the University Human Ethics Committee and performed according to the Declaration of Helsinki. All subjects had participated in previous studies in this laboratory utilizing both FI and SP exercise and thus they were fully familiarized with all experimental procedures.

5.2.3: *Preliminary Session*

Approximately 1 week before the first experimental trial, subjects reported to the laboratory for anthropometric measurements, and submaximal and $\dot{V}O_{2\max}$ testing. This session was conducted in a moderate environment ($20.6 \pm 2.0^{\circ}\text{C}$), with the exercise tests taking place on an electronically braked cycle ergometer (Lode Excalibur, Groningen, The Netherlands) set in the pedal rate independent mode. All subsequent exercise tests were completed on the same cycle ergometer. The tests first required the subjects to cycle for 6 min at each of four consecutive submaximal power outputs (100 W, 150 W, 200 W, and 250 W). Approximately five minutes after completion of the 250 W stage, during which time the subjects rested, an incremental exercise test (45 W/min) to volitional exhaustion was completed. A linear relationship between the mean rate of

oxygen consumption during the last two minutes of each submaximal stage and power output was determined. This equation was used to calculate a power output which would elicit 70% of $\dot{V}O_2$ max for each subject, and was later used to construct the exercise protocols.

5.2.4: Experimental Protocol

Approximately 7 days following the preliminary session, subjects arrived at the laboratory to complete their FI trial, which was followed 7 days later by their SP trial. All trials took place in a hot and dry environmental chamber: ambient temperature, $40.6 \pm 0.2^\circ\text{C}$; relative humidity, $23 \pm 3\%$. In order to control for the total amount of work completed it was impossible to randomize the two trials, and therefore subjects were not blinded to which trial they completed. Although no attempt was made to deceive the subjects they were made completely unaware of the research hypotheses and the purpose of the study. Although all testing was completed during the southern hemisphere summer months, it was assumed that the subjects were not heat acclimatized as outdoor temperature averaged only $19 \pm 4^\circ\text{C}$.

Pre-trial diet and hydration were controlled and confirmed as mentioned previously (*see Chapter Four*). Further activity and diet standardization was achieved via a standardized training ride 60 min in duration at a moderate intensity ($74 \pm 7\%$ heart rate max) the day before each trial (~24 h) and by the subjects consuming a standardized meal 3 h prior to the experimental trial. Subjects were not allowed to drink during the trials and wore only cycling shorts and shoes.

Prior to arrival the subjects ingested a core body temperature pill, and upon arrival at the laboratory, a cannula was inserted into an antecubital vein and kept patent with saline. The subjects then voided and nude body weight was measured. A HR monitor and skin thermistors were applied, and the subjects then entered the environmental chamber for completion of the experimental trial. Upon completion of exercise the subjects were promptly removed from the chamber, and the HR monitor and skin thermistors were

removed. Nude body weight was measured following towel drying, after which the cannula was removed.

5.2.5: Experimental Procedures

5.2.5.1: Cycling Exercise

A standard 5 min warm-up (at 150 W) in the environmental chamber was followed immediately by either FI or SP. In both trials subjects were verbally encouraged at random intervals by the same researcher and were unaware of elapsed time, HR, or (in FI only) work completed. During SP, subjects were informed of the amount of work completed at intervals that corresponded with the taking of measurements (see below). Exercise continued until one of the following conditions occurred: 1) voluntary exhaustion, 2) T_C reached 40.0°C, 3) the subject displayed signs and/or symptoms of heat stroke (Armstrong et al. 2007), or 4) (in SP only) the required amount of work had been completed.

FI required subjects to cycle at a fixed power output calculated to elicit 70% ($70.8 \pm 6.4\%$) of $\dot{V}O_{2max}$ until one of the previously mentioned conditions had been met. During FI power output was independent of cycling cadence. SP required subjects to complete as quickly as possible the same amount of work as completed in FI. However, during SP power output was proportionate to cycling cadence in a relationship defined by the linear factor. From the data collected during the preliminary session, this linear factor was calculated for each subject as follows: $LF = PO_{70\%} / (rpm)^2$, where LF is the linear factor, $PO_{70\%}$ is the power output that would elicit 70% of $\dot{V}O_{2max}$, and rpm is the optimal cycling cadence chosen by each subject.

Immediately prior to commencement, during, and upon completion of exercise, exercise time (SP only), HR, mean skin temperature (\bar{T}_{sk}), T_C , thermal discomfort, thermal sensation, and RPE were recorded every 3 min during FI and at the same amount of work completed during SP (irrespective of time). Cardiovascular and metabolic responses were measured at the first recording interval (FI: at 3 min; SP: after $15 \pm 4\%$ of the

required work had been completed) and immediately prior to exhaustion (FI) / completion (SP; 100% of the required work had been completed). Blood glucose and lactate were measured prior to exhaustion/completion, while percent changes in plasma volume and whole body sweat rate were determined pre- to post-exercise. In SP, power output was calculated from the amount of time it took to complete the required amount of work.

5.2.5.1: Measurements

Anthropometric characteristics, heart rate, \bar{T}_{sk} , RPE, thermal discomfort and thermal sensation were measured as described previously (*see Chapter Four*).

Cardiac output (\dot{Q}) was estimated via the indirect Fick equation: $\dot{V}CO_2 = \dot{Q}/A - V CO_2$ where: $\dot{V}CO_2$ is the rate of carbon dioxide elimination and A-V CO_2 is the arteriovenous CO_2 content difference. $\dot{V}CO_2$ was measured from the expired gases (see below) while A-V CO_2 was calculated from the estimated venous and arterial PCO_2 (McHardy 1967). Arterial PCO_2 was estimated from the end-tidal CO_2 data (PET CO_2) measured prior to the rebreathing procedure and corrected as demonstrated by Jones et al. (1979), while venous PCO_2 was estimated via the CO_2 rebreathing method described by DeFares (1958) and corrected according to Paterson and Cunningham (1976). The CO_2 rebreathing procedures involved the subjects rebreathing from an anaesthesia bag filled with a gas mixture containing 4% CO_2 , 35% O_2 , and the balance nitrogen. The volume of this rebreathing bag was approximately that of tidal volume as measured during the preliminary session. The high O_2 concentration utilized presently was employed in order to minimize hypoxemia, assuring full oxygenation of the blood during rebreathing (Ohlsson and Wranne 1986). The rebreathing procedure commenced when the PET CO_2 values were stable, upon which the rebreathing valve was opened and the rebreathing commenced. CO_2 rebreathing lasted approximately 15 s, during which an exponential capnograph tracing was produced, allowing for estimation of venous PCO_2 (DeFares 1958). All PET CO_2 data were measured (O_2/CO_2 Gas Analyzer, ADInstruments, Australia), acquired (PowerLab, ADInstruments, Australia), and displayed (Chart5, ADInstruments, Australia) continuously throughout the entire procedure. Stroke volume

was calculated from the Fick equation. Blood pressure was measured in duplicate manually using a stethoscope and a sphygmomanometer over the right brachial artery. All blood pressure measurements were made by the same experienced operator. Mean arterial pressure (MAP, in mmHg) was estimated by auscultation of the systolic (SBP) and diastolic blood pressure (DBP) according to the following equation: $MAP = DBP + 1/3 * (SBP - DBP)$.

Expired gases were collected for one minute via standard Douglas bags. The expired gases were analyzed for CO₂ and O₂ concentrations (AEI Technologies, USA) and volume (dry gas meter, Harvard, UK) and values converted to STPD. Rates of O₂ uptake ($\dot{V}O_2$), $\dot{V}CO_2$, respiratory exchange ratio, and expiratory minute ventilation were calculated.

According to previously reported guidelines (Byrne and Lim 2007), subjects ingested a calibrated telemetric core body temperature sensor (CorTemp™, Palmetto FL, USA) 6 h prior to their experimental trial, which served as an indication of T_C. In the present study increased thermoregulatory strain is any combination of an increased rate of rise of T_C or higher T_C at exhaustion/completion.

The modified PSI was used as an indicator of the combined thermoregulatory (T_C) and cardiovascular (HR) strain (Moran et al. 1998), and was calculated to directly compare to the results in the pilot analysis. PSI was calculated as follows: $PSI = 5 \cdot (T_{Ct} - T_{Co}) / (40.0 - T_{Co}) + 5 \cdot (HR_t - HR_o) / (HR_{max} - HR_o)$ where: T_{Co}, resting core temperature (°C); T_{Ct}, core temperature at exhaustion (FI) or completion (SP; °C); HR_o, resting heart rate (bpm); HR_t, heart rate at exhaustion (FI) or completion (SP; bpm); HR_{max}, max heart rate measured during the $\dot{V}O_2$ max test.

The Heat Strain Index (HSI) served as an estimate of the thermal compensability of the environment, where an HSI > 1.0 indicates uncompensable heat stress, and an HSI < 1.0 indicates a compensable thermal environment (Cheung et al. 2000). The HSI was calculated as the ratio of the required evaporative cooling for heat balance (\dot{E}_{req} ; in W/m²)

and the maximal evaporative capacity of the environment (\dot{E}_{\max} ; in W/m^2) (Belding and Hatch 1955). \dot{E}_{req} was calculated in the following manner (Cheung et al. 2000): $\dot{E}_{\text{req}} = \dot{M} - \dot{W} \pm (\dot{C} + \dot{R}) \pm (\dot{C}_{\text{res}} + \dot{E}_{\text{res}})$ where: \dot{M} is the rate of metabolic heat production (in W/m^2), calculated as follows (Kenney 1998): $\dot{M} = (352 \cdot (0.23 \cdot \text{RER} + 0.77)) \cdot \dot{V}\text{O}_2 / \text{BSA}$. \dot{W} is the rate of energy transfer from the generation of external work (in W/m^2). $\dot{C} + \dot{R}$ is the rate of heat transfer from convection (\dot{C} ; in W/m^2) and radiation (\dot{R} ; in W/m^2), calculated as the sum of: $\dot{C} = h_c \cdot (\bar{T}_{\text{Sk}} - T_A)$ (Kerslake 1972) and $\dot{R} = 4.7 \cdot (T_A - \bar{T}_{\text{Sk}})$ (Kenney 1998) where: h_c is the convective heat transfer coefficient (in $\text{W/m}^2/^\circ\text{C}$) (Kerslake 1972) and T_A is the ambient temperature (in $^\circ\text{C}$). $\dot{C}_{\text{res}} + \dot{E}_{\text{res}}$ is the rate of respiratory conductive (\dot{C}_{res}) and evaporative (\dot{E}_{res}) heat transfer and was calculated as follows (Kenney 1998): $\dot{C}_{\text{res}} + \dot{E}_{\text{res}} = (0.0012 \cdot \dot{M} \cdot (34 - T_A)) + (0.0023 \cdot \dot{M} \cdot (44 - P_A))$ where P_A is ambient vapor pressure (in kPa). \dot{E}_{\max} was calculated according to the following equation (Kerslake 1972): $\dot{E}_{\max} = \text{LR} \cdot h_c \cdot (P_{\text{Sk}} - P_A)$ where LR is the Lewis Relation (16.5°C/kPa) and P_{Sk} is the saturated vapor pressure at the skin (in kPa). Additionally, evaporative heat loss (\dot{E} ; in W/m^2) was estimated according to the following equation (Kerslake 1972): $\dot{E} = (P_{\text{Sk}} - P_A) \cdot v^{0.5} \cdot 124$ where v is air velocity (0.5 m/s).

After correcting for respiratory and metabolic water losses (Mitchell et al. 1972), changes in nude body weight were used to estimate whole body sweat rate according to the following equation: Whole body sweat rate (in g/min) = (Initial body weight - final body weight) + ($\dot{V}\text{O}_2 \cdot (\text{RER} \cdot 1.96 - 1.43)$) + ($0.019 \cdot \dot{V}\text{O}_2 \cdot (44 - P_A)$).

Whole blood lactate and glucose were assayed using a YSI lactate analyzer (Yellow Springs, OH, USA) and an Accu-Check Advantage glucose meter (Mannheim, Germany). Whole blood hemoglobin and hematocrit were measured via an automated analyzer (ABL800 FLEX, Radiometer, Denmark). Percentage changes in plasma volume were calculated according to previously described methods (Dill and Costill 1974).

5.2.6: Statistical Analysis

Each subject completed a different amount of work and therefore it was not possible to statistically compare 'raw' power output responses over time and between trials. Accordingly, for each subject during each trial, power outputs during SP and FI were standardized and compared by analyzing the log transformed relationship between time (dependent variable) and the cumulative work completed (independent variable) for each subject during each trial. Both time and cumulative work completed were log transformed and these data were fit with a significant ($P < 0.001$; $R^2 = 0.99 \pm 0.00$) linear regression model [$y = y_0 + a \cdot x$]. For all subjects, the mean y-intercept (Y_0) and slopes (a) in the two conditions were compared via paired *t*-tests. This analysis transformed the changes in power output during SP linear allowing for statistical comparison with FI. These data were analyzed using SigmaPlot statistical software (v. 10.0, Systat Software Inc. Chicago, IL, USA).

Mean differences between trials were compared via paired *t*-tests. To identify any changes in the cardiovascular, metabolic, and heat exchange variables over time during exercise, a two-way (trial x time) repeated measures analysis of variance (ANOVA) was also conducted. These data were assessed for approximation to a normal distribution and sphericity, and no corrections were necessary. These data were analyzed using SPSS statistical software (V. 17, Chicago, IL, USA). *A priori* statistical significance was set at $P < 0.05$. All data are reported as mean \pm SD unless noted otherwise.

There was a large discrepancy in the amount of work completed during FI, and therefore SP (range: 232 - 312 kJ). Accordingly, the 3 min fixed measurement period corresponded to a higher or lower percentage of work completed per subject, with each subject ultimately having a different number of data points depending upon their time to exhaustion in FI. Consequently, it was not possible to analyze or display mean data *during* the exercise bout other than at the start (i.e. at $15 \pm 4\%$ of the required work completed) and at completion / exhaustion (i.e. at 100% of the required work completed). Figure 5.2 demonstrates the typical observed responses of selected variables during both trials.

5.3: Results

5.3.1: Exercise Duration and Power Output

Seven (of eight) subjects exercised until voluntary exhaustion in FI, while exercise was stopped for 1 subject upon the attainment of a T_C of 40.0°C. In SP, all subjects successfully completed the required amount of work. In both trials subjects completed 281 ± 32 kJ of work, however, SP took ~12% longer ($P < 0.001$) than FI (Table 5.2). Accordingly, mean power output was higher ($P < 0.001$) in FI (234 ± 25 W) than in SP (207 ± 23 W; Figure 5.1). Relative to FI, power output slowed ($P < 0.05$) over time in SP (Table 5.3).

Table 5.2: Physiological measures upon exercise exhaustion/completion (mean \pm SD).

	Exercise Duration (min)	T_C (°C)	PSI	RPE	Blood Lactate (mmol/L)	Blood Glucose (mmol/L)
Fixed-Intensity	20.3 \pm 3.4*	39.4 \pm 0.3*	9.1 \pm 0.9*	18 \pm 2*	2.9 \pm 0.8*	6.1 \pm 0.5
Self-Paced	23.2 \pm 4.1	39.1 \pm 0.4	8.3 \pm 1.1	16 \pm 2	2.3 \pm 0.7	5.8 \pm 0.3

T_C (°C), core body temperature; PSI, Physiological Strain Index. * denotes significantly different than self-paced ($P < 0.05$).

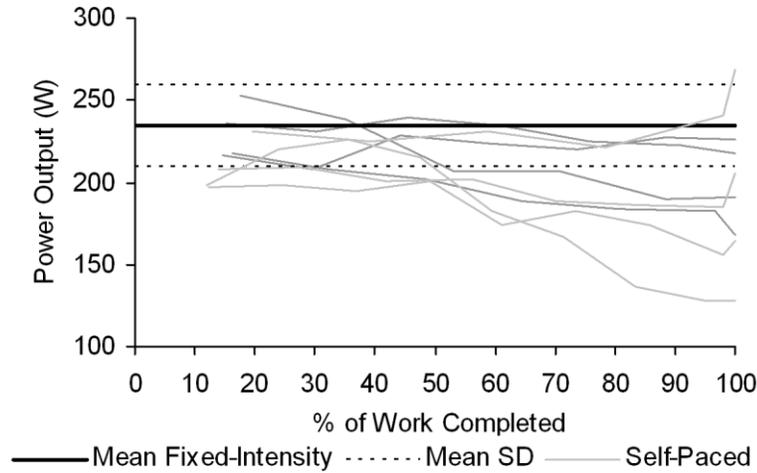


Figure 5.1: Power output during fixed-intensity (mean fixed-intensity \pm SD) and self-paced exercise. Each self-paced line represents data from one subject.

Table 5.3: Mean linear regression model¹ data for the log transformed relationship between time and the cumulative work completed (mean \pm SD).

	a	y0
Fixed-Intensity	1.000 \pm 0.0000 *	1.1455 \pm 0.0450
Self-Paced	0.9651 \pm 0.0361	1.1423 \pm 0.0419

¹ [y=y0+a*x]; a, mean slope; Y0, mean y-intercept. * denotes significantly different than self-paced (P<0.05).

5.3.2: Temperature Regulation and Heat Exchange

Pre-exercise T_C was similar ($P>0.05$) in FI (37.2 ± 0.2 °C) and SP (37.2 ± 0.2 °C). The rate of rise in T_C during exercise was higher ($P<0.01$) in FI (0.108 ± 0.020 °C/min) than in SP (0.082 ± 0.016 °C/min), with T_C being higher ($P<0.05$) at exhaustion in FI (Table 5.2).

A typical T_C response during both trials is presented in Figure 5.2. Average \bar{T}_{Sk} was similar ($P>0.05$) in both FI (37.4 ± 0.3 °C) and SP (37.4 ± 0.3 °C). The compensability of the thermal environment and body heat exchange are presented in Table 5.4 and Figure 5.3.

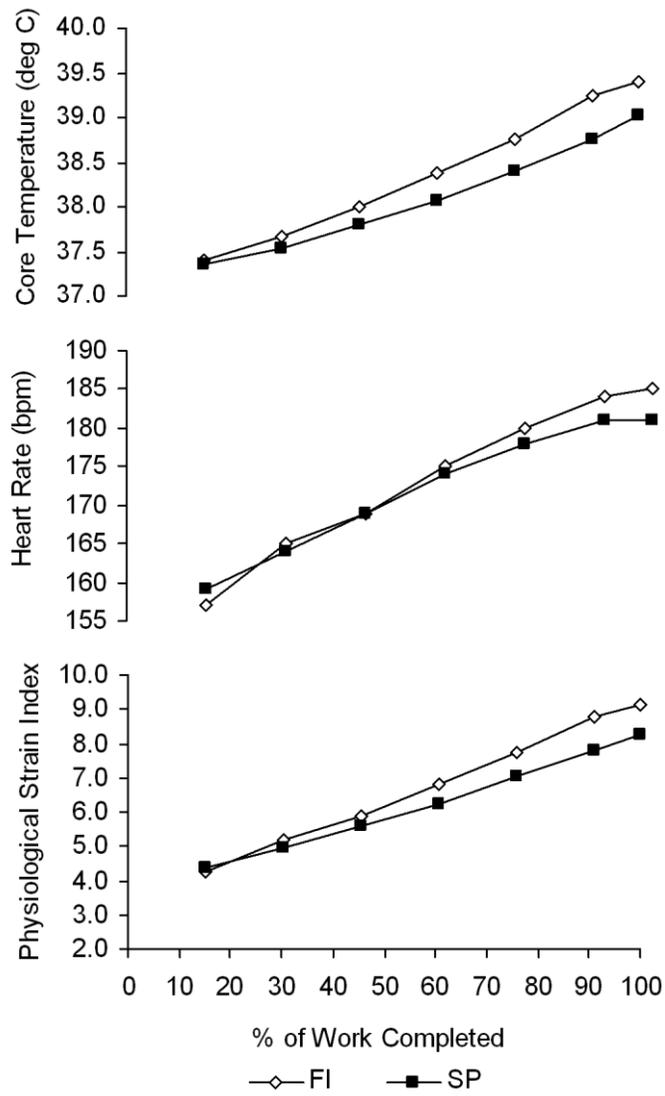


Figure 5.2: Core temperature, heart rate, and physiological strain responses in one subject during both fixed-intensity (FI) and self-paced (SP) exercise.

Table 5.4: Thermal compensability during fixed-intensity and self-paced exercise in the heat (mean \pm SD).

	Percentage of Total Work Completed			
	15%		100%	
	Fixed-Intensity	Self-Paced	Fixed-Intensity	Self-Paced
\dot{E}_{req} (W/m ²)	627 \pm 86	585 \pm 92	593 \pm 81*	550 \pm 63
\dot{E}_{max} (W/m ²)	406 \pm 57	385 \pm 22	421 \pm 24	421 \pm 19 †
HSI	1.58 \pm 0.34	1.52 \pm 0.24	1.41 \pm 0.22	1.31 \pm 0.14 †

\dot{E}_{req} (W/m²), required evaporative cooling for heat balance; \dot{E}_{max} (W/m²), maximal evaporative capacity of the environment; HSI, heat strain index. * denotes significantly different than self-paced (P<0.05); † denotes significantly different than 15% (P<0.05).

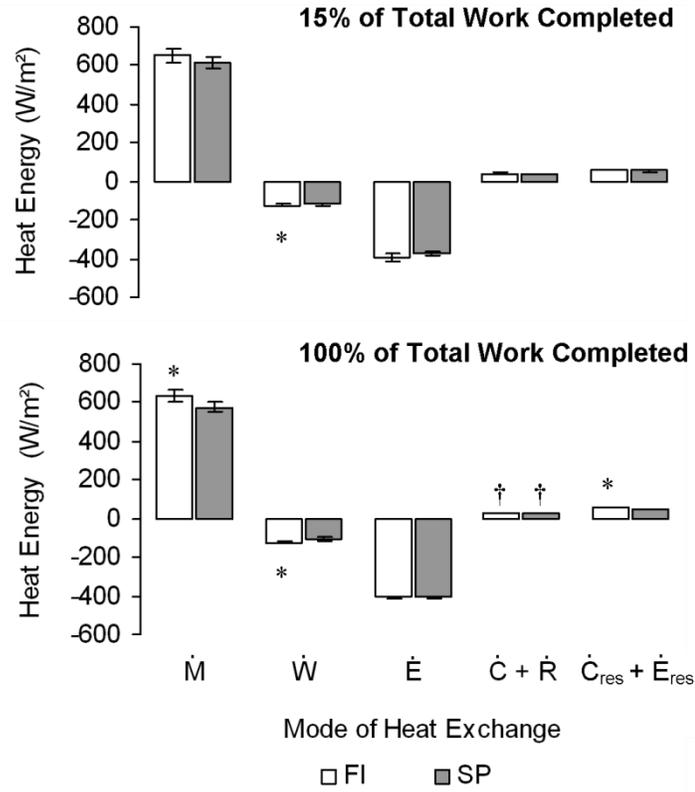


Figure 5.3: Rates and modes of heat exchange (Mean \pm SE) during (at 15% of total work completed) and upon exhaustion/completion (100% of total work completed) of fixed-intensity (FI) and self-paced (SP) exercise. \dot{M} , rate of metabolic heat production; \dot{W} , rate of heat transfer from the generation of external work; \dot{E} , rate of heat transfer from evaporation; $\dot{C} + \dot{R}$, the sum of the rates of heat transfer from convection (\dot{C}) and radiation (\dot{R}); $\dot{C}_{res} + \dot{E}_{res}$, the sum of respiratory conductive (\dot{C}_{res}) and evaporative (\dot{E}_{res}) rates of heat transfer. * denotes significantly different than SP ($P < 0.05$); † denotes significantly different than 15 % ($P < 0.05$).

5.3.3: Cardiovascular Responses and Physiological Strain

Pre-exercise HR was similar ($P > 0.05$) in FI (71 ± 8 bpm) and SP (69 ± 12 bpm). MAP, \dot{Q} , SV and HR data during exercise are presented in Figure 5.4. PSI was higher ($P < 0.01$) at the end of FI (Table 5.2). Typical responses during each trial are presented in Figure 5.2.

5.3.4: Metabolic and Fluid Balance Measures

$\dot{V}O_2$ was similar ($P>0.05$) upon completion of 15% of the required work (FI: 3.50 ± 0.45 L/min, SP: 3.28 ± 0.47 L/min), but was higher ($P<0.05$) in FI upon exhaustion/completion (FI: 3.39 ± 0.50 L/min: SP: 3.11 ± 0.41 L/min). Blood glucose and lactate at exhaustion/completion are presented in Table 5.2. Percent changes in plasma volume (FI: $-8.9 \pm 6.9\%$, SP: $-6.6 \pm 4.4\%$) and whole body sweat rates (FI: 13.5 ± 1.3 g/min; SP: 12.7 ± 2.7 g/min) were similar ($P>0.05$) between the two trials.

5.3.5: Perceptual Measures

RPE was higher ($P<0.05$) upon exhaustion/completion in FI (Table 5.2). In both conditions completion/exhaustion was unanimously ($P>0.05$) regarded as very uncomfortable (4.0 ± 0.0) and hot (7.0 ± 0.0).

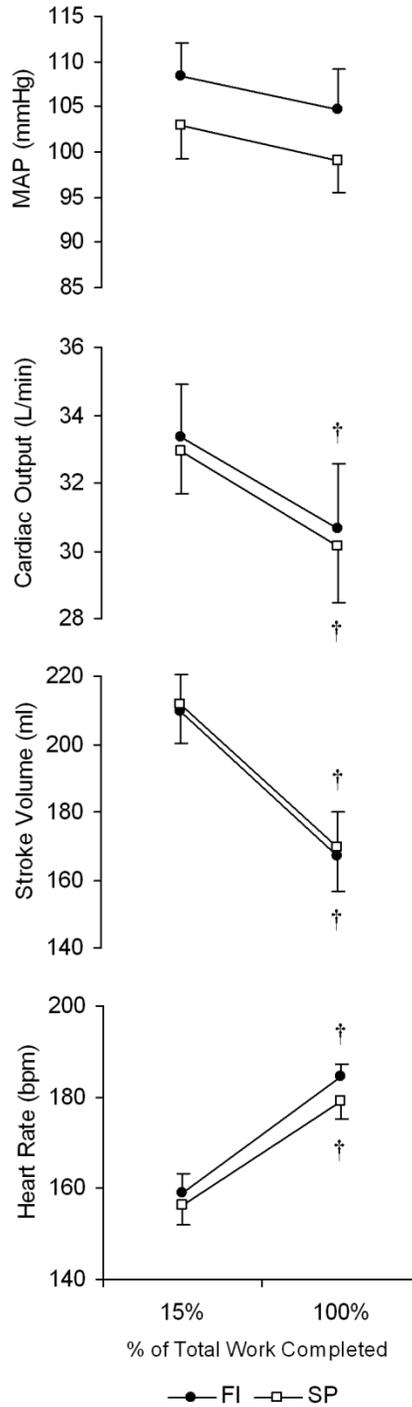


Figure 5.4: Mean arterial pressure (MAP), cardiac output, stroke volume and heart rate (Mean \pm SE) during (at 15% of total work completed) and upon completion (100% of total work completed) of fixed-intensity (FI) and self-paced (SP) exercise. * denotes significantly different than SP ($P < 0.01$); † denotes significantly different than 15 % ($P < 0.05$).

5.4: Discussion

This study is the first to formally evaluate exercise modality as a modulator of body temperature regulation in the heat. By comparing the thermoregulatory, cardiovascular and heat exchange responses during work-matched, fixed-intensity and self-paced exercise in uncompensable heat, it was found that voluntary reductions in power output during self-paced exercise improved thermal compensability and extended exercise duration. Additionally, thermoregulatory and physiological strain was higher during and upon completion of fixed-intensity exercise. Surprisingly however, differences in cardiovascular responses between exercise modalities were not observed.

Relative to fixed-intensity exercise, in Study B we found that when exercise was self-paced power output was gradually reduced with exercise duration (Figure 5.1). This was demonstrated by the log transformed relationship between time and cumulative work completed. This analysis showed that the power outputs were similar upon exercise commencement (i.e. the mean y-intercepts were similar), yet became reduced over time during the self-paced trial (i.e. the mean slope was lower than that during the fixed intensity trial; Table 5.3). Ultimately, this reduction in power output resulted in a longer exercise duration in the self-paced trial (Table 5.2). Previously, exercise intensity has generally been found not to differ between self-paced and fixed-intensity trials undertaken in a moderate thermal environment (Billat et al. 2001; Billat et al. 2006; Lander et al. 2009). In fact, there is some evidence that exercise performance, and therefore intensity, is actually improved (faster) when exercise is self-paced compared to that during fixed-intensity exercise (Garcin et al. 2008). This discrepancy is likely due to the uncompensable heat stress in which our trials were conducted.

Generally, in moderate thermal conditions, fixed-intensity exercise has previously been found to be more physiologically stressful than self-paced exercise despite a similar exercise intensity (Billat et al. 2006; Lander et al. 2009). These studies indicated that a similar exercise intensity elicited significant reductions in mean oxygen uptake and heart rate (Billat et al. 2006), core body temperature (Lander et al. 2009), neuromuscular activity (Lander et al. 2009), and post-exercise blood lactate concentrations (Billat et al.

2006; Lander et al. 2009). These findings are not unanimous however (Garcin et al. 2008). Indeed, a pilot analysis of the previously published literature indicated that, in the heat, physiological strain is higher at the end of fixed-intensity when compared to self-paced exercise. This was mediated predominantly by the elevation in core temperature and not heart rate, as heart rate was actually higher at completion of the self-paced exercise (Table 5.1). Similar results were also found experimentally. An increased rate of rise in core temperature during exercise and higher core temperatures, blood lactate concentrations, and perception of effort upon exhaustion/completion (Table 5.2) additionally supports the contention that self-paced exercise is less physiologically demanding than fixed-intensity exercise.

This study has also demonstrated that modification of body heat exchange (Figure 5.3) and the corresponding improvement in thermal compensability (Table 5.4) successfully allowed the same exercise task to be completed with less thermoregulatory strain (Table 5.2; Figure 5.2). Given that the rate of evaporative heat loss was similar and that the rates of conductive and radiative heat gain changed similarly between trials (Figure 5.3), the compensability improvement was likely a direct result of the observed reductions in the rate of metabolic heat production (Figure 5.3). Differences in the rates of respiratory conductive and evaporative heat transfer were observed upon completion/exhaustion (Figure 5.3). However, these are almost certainly driven by the observed differences in oxygen uptake, and therefore the rate of metabolic heat production. It is important to note that while the compensability of the environment was improved at the end of the self-paced trial, it was still considered uncompensable (Table 5.4). This observation is likely due to methodology utilized. For instance, the subjects were instructed to successfully complete the given amount of work as quickly as possible; therefore it is likely they compromised heat gain for exercise performance (e.g. Cabanac 1992), thus making true thermal compensability impossible during the relatively short period of exercise.

It is notable that heat balance was not attained (i.e. $\dot{M} - \dot{W} \neq \dot{C} + \dot{R} + \dot{E} + \dot{C}_{res} + \dot{E}_{res}$) in either the self-paced or fixed-intensity trials. It has been suggested previously that, when

given the freedom to self-pace, subjects decrease their exercise intensity in order to ultimately reduce the rate of rise in body heat storage to zero (Tucker et al. 2006). Given the reduced rate of rise in core temperature and, upon completion/exhaustion, a lower core temperature (Table 5.2) and rate of metabolic heat production (Figure 5.3), the present study certainly supports that the rate of heat storage is reduced when self-paced exercise is undertaken in the heat. Nevertheless, given that it was not the intent of this study to identify the physiological signals initiating reductions in intensity during self-paced exercise, this study does not allow for further speculation.

Unexpectedly, no differences between exercise modalities were observed for the cardiovascular responses measured during the initial stages of exercise or upon completion/exhaustion (Figure 5.4). Nevertheless, given that reductions in power output (Figure 5.1, Table 5.3), metabolic heat production (Figure 5.3), and oxygen uptake were observed during self-paced exercise, it would be naïve to conclude there were not slight differences in oxygen delivery. Therefore, it is highly likely that the CO₂ rebreathing methodology (Defares 1958) used to estimate cardiac output may not have been sensitive enough to observe these differences. This aside, the observed increase in heart rate, and decreases in stroke volume and cardiac output (Figure 5.4) are typical characteristics of prolonged exercise in the heat associated with marked dehydration and hyperthermia (Gonzalez-Alonso et al. 2000; Gonzalez-Alonso et al. 1995).

5.6.1: Considerations and Limitations

These studies support exercise modality as a modulator of body temperature regulation. Compared to that during fixed-intensity exercise, during self-paced exercise behavioral reductions in the rate of metabolic heat production (Figure 5.3) apparently reduced the rate of rise in core temperature, allowing the same amount of work to be completed but with less thermoregulatory strain (Table 5.2). These findings support the hypothesis of a thermoregulatory continuum. For example, in the present paradigm behavior was preferentially elicited (i.e. self-paced exercise), however during instances where behavior is restricted (i.e. fixed-intensity exercise), when the signaling inputs to behave are ignored, or when behavior is inadequate, heat exhaustion ensues. It is only upon the

failure of both behavior and exhaustion that temperature regulation may be lost, homeostasis compromised, and exertional heat stroke becomes imminent. This is supported by the high incidence of exertional heat stroke when high motivation and external factors (e.g. a drill sergeant, coach, fellow runners, etc.) dictate exercise intensity (Armstrong et al. 2007; Epstein et al. 1999; Shibolet et al. 1976) and a lower incidence when people exercise alone or self-pace (Brake and Bates 2002a).

Notably, this behavioral arrangement is similarly reflected by that of the thermoregulatory system at rest (c.f. Cheung and Flouris 2009). At rest, behavior is preferentially initiated by changes in skin temperature, thereby preventing changes in core temperature (Schlader et al. 2009). It is only when behavior is restricted or insufficient that core temperature rises and energy/water consuming autonomic thermoregulatory responses are elicited (Romanovsky 2007). In the circumstance that both behavioral and autonomic thermoregulatory responses are inadequate, core temperature will rise/fall uncontrollably, and body temperature regulation may be lost.

Given that it was not possible to work-match *and* randomize the experimental trials, it must be acknowledged that the non-randomized experimental design may have impacted the results. These effects were minimized by using well familiarized subjects and by blinding them to the research hypotheses and the purpose of the study. Ultimately, this non-randomized repeated measures experimental design was deemed the sole means in which to test the hypotheses, and therefore any potential order effect was deemed acceptable. Additionally, given that intestinal temperature is slower to react to changes in body temperature than other indices of core temperature, e.g. esophageal temperature (Byrne and Lim 2007), it is acknowledged that intestinal temperature measurement may have underestimated the actual changes. Furthermore, it is also acknowledged that the methods used to estimate body heat exchange are less sensitive than those of calorimetry. Notably however, these facilities are rare. It is suggested that future investigations in this area account for these limitations.

5.6.2: Conclusions

The data presented indicate that under uncompensable heat stress exercise modality is a modulator of body temperature regulation. Compared to fixed-intensity exercise, it has been shown that, when given the opportunity to self-pace, reductions in exercise intensity decrease the rate of metabolic heat production, and thus improve the compensability of the thermal environment. Consequently, when the same exercise task was completed when exercise intensity is either fixed or freely adjustable, exercise was accompanied by lower levels of thermoregulatory strain when exercise was self-paced. In conclusion, this study presents experimental evidence of a formal relationship between the physiological outcomes observed during and upon completion/exhaustion of self-paced and fixed-intensity exercise in the heat.

Acknowledgements

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CHAPTER SIX

6.0: Evidence for Thermoregulatory Behavior during Self-Paced Exercise in the Heat

Publication(s) based on this chapter:

Schlader ZJ, Stannard SR, Mundel T. (2011) Evidence for thermoregulatory behavior during self-paced exercise in the heat. *J Therm Biol* 36: 390-396.

Abstract

The primary objective of this investigation was to test the hypothesis that voluntary reductions in exercise intensity in the heat improve heat exchange between the body and the environment, and are thus, thermoregulatory behaviors. This was accomplished by observing the conscious selection of exercise intensity and the accompanying thermal outcomes of eleven moderately active males when exposed to an uncompensably hot (UNCOMP) and a compensable (COMP) thermal environment. Evidence for thermoregulatory behavior was defined relative to the specific, pre-determined, definition. Self-selected exercise intensity (power output) was unanimously reduced ($P < 0.001$) in UNCOMP over time and relative to COMP in all subjects, by $21 \pm 5\%$ (mean \pm SD). These voluntary responses were found to modify ($P < 0.05$) metabolic heat production over time and therefore heat exchange ($P < 0.05$) between the body and the environment. Likewise, the observed reductions in power output were, at least in part, due to a conscious action, which were found to be inversely related to total body heat storage ($r = -0.994$) and thermal discomfort ($r = -0.953$). There was no evidence for thermoregulatory behavior in COMP. These data uniquely indicate that voluntary reductions in exercise intensity improve heat exchange over time, and therefore contribute to the regulation of body temperature. By association, these findings suggest that reductions in exercise intensity in the heat are, by definition, thermoregulatory behaviors.

Keywords

Thermal behavior, Exercise intensity, Thermal discomfort, Thermal compensability

6.1: Introduction

Behavior is generally thought to be the most effective form of temperature regulation (Parsons 2003) and compared to the relatively restricted capacity of the autonomic thermoregulatory responses, behavioral responses are nearly limitless (Benzinger 1969). Thus, behavior is regarded as the ‘first line of defense’ in maintaining body temperature (Werner et al. 2008). However, difficulty in determining functional relationships between thermal stressors and the ensuing behavior means that relatively little is known about the control of human thermoregulatory behavior. Hence, the development of models to evaluate thermal behavior in humans is of importance.

A notable example of thermoregulatory behavior in humans is voluntary exercise (Mercer 2001). This is observed most commonly when a person voluntarily increases heat production by exercising when cold (Caputa and Cabanac 1980). Interestingly, the selected intensity of this exercise is inversely related to ambient temperature (Cabanac and Leblanc 1983). Therefore, it is perhaps not surprising that exercise intensity is voluntarily reduced in the heat (Budd 2001; Ely et al. 2010; Tattersson et al. 2000; Tucker et al. 2004). Thus, self-paced exercise under environmental stress has been suggested to provide meaningful information concerning the control of thermal behavior in humans (Flouris 2010). However, in order to assert self-paced exercise in the heat as a model to evaluate human thermoregulatory behavior, a thorough investigation of the behavioral and thermal outcomes of the voluntary selection of exercise intensity in the heat is warranted.

The primary objective of this investigation was to test the hypothesis that voluntary reductions in exercise intensity in the heat modify heat exchange between the body and the environment, and are thus, thermoregulatory behaviors. This was accomplished by observing the conscious selection of exercise intensity during exposure to an uncompensably hot (UNCOMP) and a compensable (COMP) thermal environment.

Within this uncompensable heat stress paradigm, as the autonomic capability for heat exchange is maximized and autonomically induced heat balance is impossible (Cheung et al. 2000), it was assumed that any modification of heat exchange over time must be driven by alterations in exercise intensity (**Chapter Five**).

6.2: Methods

6.2.1: Experimental Overview

In UNCOMP and COMP, eleven male volunteers each completed self-paced exercise bouts on a cycle ergometer. The subjects were instructed to complete as much work as possible in 30 min. Power output was a function of the self-selected cycling cadence and the selected ergometer load. All trials took place at the same time of day and there were seven days between each trial. A randomized experimental design was utilized in order to minimize any order effects.

6.2.2: Subjects

Eleven healthy, physically active males agreed to participate in the study. The subjects' characteristics were (mean \pm SD): age, 23 \pm 3 y; height, 1.8 \pm 0.1 m; weight, 71.6 \pm 7.0 kg; body surface area, 2.00 \pm 0.18 m²; percent body fat, 11.3 \pm 4.1%; $\dot{V}O_2$ max, 4.59 \pm 0.82 l/min. Given that aerobically well-trained subjects have an altered perception of their physiological thermal strain during exercise (Tikusis et al. 2002) well-trained subjects were excluded, thereby minimizing inter-subject variability. All subjects exercised a minimum of 3 days per week, but were not taking part in any formal exercise training. Each subject was fully informed of the experimental procedures and possible risks before giving informed, written, consent. The protocol was approved by the University Human Ethics Committee and performed according to the Declaration of Helsinki.

6.2.3: Preliminary Sessions

Approximately two weeks before the first experimental trial, subjects reported to the laboratory for a $\dot{V}O_2$ max test. This test was performed in a moderate environment (20.4

$\pm 0.4^{\circ}\text{C}$) on a friction braked cycle ergometer (Monark 818, Sweden). Via a custom built interface, the cycling cadence, ergometer load, and corresponding power output, were acquired (PowerLab, ADInstruments, Australia), recorded (Chart5, ADInstruments, Australia) and displayed continually. Changing the ergometer load involved turning a dial located on the ergometer. All exercise tests were completed on this same ergometer. During the $\dot{V}\text{O}_2\text{max}$ test subjects were required to maintain a self-selected cycling cadence (mean: 91 ± 6 rpm), while the researcher adjusted the ergometer load accordingly. This incremental exercise test commenced at a power output of 100 W and increased by 50 W every 2 min in a stepwise manner until volitional exhaustion (c.f. Karp et al. 2006).

Approximately one week before the first experimental trial, all subjects completed a familiarization session in which they completed the same self-paced cycling exercise bout they completed in the subsequent experimental trials. This exercise bout took place in the laboratory in moderate ambient conditions ($20.1 \pm 0.9^{\circ}\text{C}$).

6.2.4: Experimental Protocol

Approximately seven days following the familiarization session subjects arrived at the laboratory to complete self-paced exercise in either COMP (Figure 6.2A) or UNCOMP (Figure 6.3A) environment. Ambient conditions in COMP were $20.4 \pm 1.2^{\circ}\text{C}$, $22 \pm 8\%$ relative humidity, while in UNCOMP they were $40.2 \pm 0.2^{\circ}\text{C}$ and $19 \pm 3\%$ relative humidity. In both COMP and UNCOMP air speed was 0.5 m/s. Due to differences in thermal sensation, the subjects could not be blinded to the conditions. Likewise, although no attempt was made to deceive the subjects they were made completely unaware of the research hypotheses. It was assumed that the subjects were not heat acclimatized as the testing was conducted during the southern hemisphere winter/spring months (mean outdoor temperature: $14 \pm 3^{\circ}\text{C}$)

Pre-trial diet and hydration were controlled and confirmed as mentioned previously (*see Chapter Four*). During the trials subjects wore only cycling shorts and shoes.

On arrival at the laboratory, the subjects voided, nude body weight was measured and a rectal thermistor was self-inserted. A heart rate monitor and skin thermistors were then applied. The subjects then entered the environmental chamber and commenced the standardized warm-up which transitioned into the self-paced exercise protocol. When the exercise bout was complete the subjects were immediately removed from the chamber, the experimental equipment was promptly removed and nude body weight was measured.

6.2.4.1: Cycling Exercise

A standardized 5 min warm-up (at 100 W) in the environmental chamber transitioned into the self-paced cycling exercise protocol. This self-paced exercise required the subjects to complete as great an amount of work as possible in 30 min. Subjects were free to change their cadence and/or the ergometer load. Subjects were verbally encouraged by the same researcher at random intervals and were aware of every 5 min time interval, but had no indication of work completed, cycling cadence, ergometer load, power output or heart rate.

Immediately prior to commencement, during, and upon completion of exercise, cycling cadence, ergometer load, power output, heart rate, mean skin (\bar{T}_{sk}) and core body (T_C) temperatures, thermal discomfort, thermal sensation, ratings of perceived exertion (RPE) and expired gases were measured and recorded every 5 min. Whole body sweat rate was determined pre- to post-exercise, while total work completed was recorded upon exercise completion.

6.2.4.2: Measurements

Anthropometric characteristics, heart rate, \bar{T}_{sk} , RPE, thermal discomfort and thermal sensation were measured as described previously (*see Chapter Four*).

Rectal temperature served as an index of T_C , and was measured with a rectal thermistor (Mon-a-therm, Tyco Healthcare Group, USA) inserted 10 cm beyond the anal sphincter.

Expired gases were collected and analyzed using an online system (Turbofit, Vacumed, USA) for two consecutive min at every recording interval. Mean rates of O₂ uptake (\dot{V}_{O_2}), CO₂ elimination, respiratory exchange ratio and expiratory minute ventilation during the final min of this collection period were used in the analysis.

The Heat Strain Index (HSI) served as an estimate of the thermal compensability of the environment, where an HSI>1.0 indicates uncompensable heat stress, and an HSI<1.0 indicates a compensable thermal environment (Cheung et al. 2000). The HSI was calculated as the ratio of the required evaporative cooling for heat balance (\dot{E}_{req} ; in W/m²) and the maximal evaporative capacity of the environment (\dot{E}_{max} ; in W/m²) (Belding and Hatch 1955). \dot{E}_{req} was calculated in the following manner (Cheung et al. 2000): $\dot{E}_{req} = \dot{M} - \dot{W} \pm (\dot{C} + \dot{R}) \pm (\dot{C}_{res} + \dot{E}_{res})$ where: \dot{M} is the rate of metabolic heat production (in W/m²), calculated as follows (Kenney 1998): $\dot{M} = (352 \cdot (0.23 \cdot RER + 0.77) \cdot \dot{V}_{O_2} / BSA$. \dot{W} is the rate of energy transfer from the generation of external work (in W/m²). $\dot{C} + \dot{R}$ is the rate of heat transfer from convection (\dot{C} ; in W/m²) and radiation (\dot{R} ; in W/m²), calculated as the sum of: $\dot{C} = h_c \cdot (\bar{T}_{Sk} - T_A)$ (Kerslake 1972) and $\dot{R} = 4.7 \cdot (T_A - \bar{T}_{Sk})$ (Kenney 1998) where: h_c is the convective heat transfer coefficient (in W/m²/°C) (Kerslake 1972) and T_A is the ambient temperature (in °C). $\dot{C}_{res} + \dot{E}_{res}$ is the rate of respiratory conductive (\dot{C}_{res}) and evaporative (\dot{E}_{res}) heat transfer and was calculated as follows (Kenney 1998): $\dot{C}_{res} + \dot{E}_{res} = (0.0012 \cdot \dot{M} \cdot (34 - T_A)) + (0.0023 \cdot \dot{M} \cdot (44 - P_A))$ where P_A is ambient vapor pressure (in kPa). \dot{E}_{max} was calculated according to the following equation (Kerslake 1972): $\dot{E}_{max} = LR \cdot h_c \cdot (P_{Sk} - P_A)$ where LR is the Lewis Relation (16.5°C/kPa) and P_{Sk} is the saturated vapor pressure at the skin (in kPa). Additionally, evaporative heat loss (\dot{E} ; in W/m²) was estimated according to the following equation (Kerslake 1972): $\dot{E} = (P_{Sk} - P_A) \cdot v^{0.5} \cdot 124$ where v is air velocity (0.5 m/s). The rate of body heat storage (\dot{S} , in W/m²) at every recording interval was calculated as follows: $\dot{S} = \dot{M} - \dot{W} + \dot{C} + \dot{R} + \dot{E} + \dot{C}_{res} + \dot{E}_{res}$. Heat storage (in kJ/m²) was calculated from \dot{S} during every 5 min period, while total body heat storage (in kJ/m²) was calculated as the cumulative sum of heat storage.

After correcting for respiratory and metabolic water losses (Mitchell et al. 1972), changes in nude body weight were used to estimate whole body sweat rate according to the following equation: Whole body sweat rate (in g/min) = (Initial body weight - final body weight) + ($\dot{V}O_2 \cdot (\text{RER} \cdot 1.96 - 1.43)$) + ($0.019 \cdot \dot{V}O_2 \cdot (44 - P_A)$).

6.2.5: Statistical Analyses

To identify any changes in dependent variables between trials and over time, a two-way (trial x time) repeated measures analysis of variance (ANOVA) was conducted. These data were assessed for approximation to a normal distribution and sphericity, and no corrections were necessary. When the two-way ANOVA revealed a significant *F* test, *post hoc* pair-wise comparisons were made incorporating a Bonferroni adjustment. Mean differences between trials were compared via paired *t*-tests. Linear regression [$y=y_0+a*x$] was used to identify trends over time in \dot{E}_{req} and \dot{E}_{max} . Within-subjected relationships between mean thermal discomfort, mean total body heat storage and mean power output were identified using Pearson product moment correlation analysis. All data were analyzed using SPSS statistical software (V. 15, Chicago, IL, USA) with *a priori* statistical significance set at $P<0.05$. All data are reported as mean \pm SD unless otherwise noted.

6.3: Results

6.3.1: Total Work and Power Output

The total amount of work completed in COMP (346.6 ± 79.7 kJ) was greater ($P<0.001$) than that completed during UNCOMP (271.5 ± 58.4 kJ). This work outcome was due to a slower ($P<0.01$) cadence (mean - UNCOMP: 94 ± 7 rpm, COMP: 98 ± 7 rpm; Figure 6.1A), lower ($P<0.001$) self-selected ergometer load (mean - UNCOMP: 1.67 ± 0.30 kP, COMP: 2.02 ± 0.53 kP; Figure 6.1B), and thus lower ($P<0.001$) power output (mean - UNCOMP: 154 ± 33 W, COMP: 201 ± 56 W; Figure 6.1C).

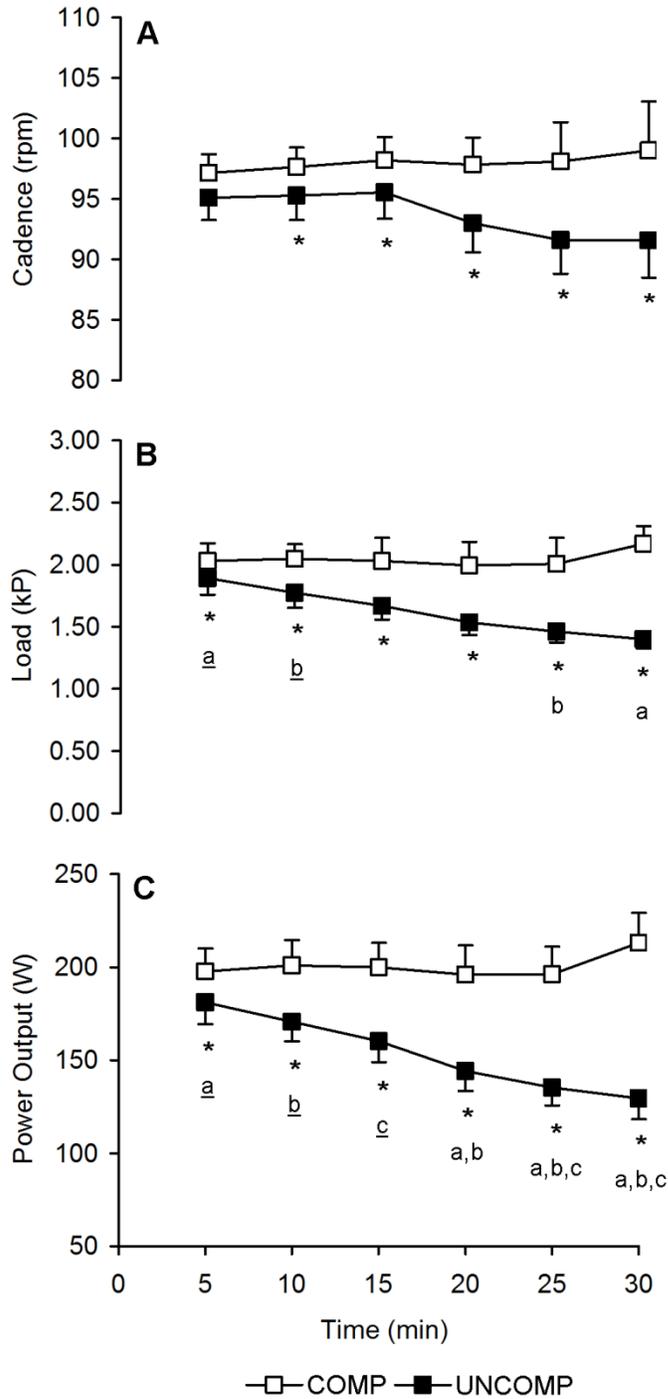


Figure 6.1: Cadence (A), ergometer load (B), and power output (C) during 30 min of self-paced exercise under uncompensable heat stress (UNCOMP) and in a compensable (COMP) thermal environment (mean \pm SE). * indicates significantly different than COMP ($P < 0.05$); letters indicate significant differences ($P < 0.05$) between underlined and the subsequent time points.

6.3.2: Temperature Regulation and Heat Exchange

Pre-exercise (i.e. pre- warm-up) T_C was similar ($P>0.05$) between trials (COMP: $37.2 \pm 0.4^\circ\text{C}$; UNCOMP: $37.2 \pm 0.4^\circ\text{C}$) and rose ($P<0.01$) similarly ($P>0.05$) in both UNCOMP ($0.046 \pm 0.016^\circ\text{C}/\text{min}$) and COMP ($0.042 \pm 0.013^\circ\text{C}/\text{min}$) through 25 min of exercise. However, final T_C (at 30 min) was higher ($P<0.05$) in UNCOMP ($38.7 \pm 0.3^\circ\text{C}$) than in COMP ($38.5 \pm 0.3^\circ\text{C}$). \bar{T}_{sk} was higher ($P<0.001$) throughout in UNCOMP (mean – UNCOMP: $37.2 \pm 0.4^\circ\text{C}$; COMP: $32.4 \pm 1.1^\circ\text{C}$), but increased ($P<0.01$) over time in both trials.

Heat loss from \dot{C} and \dot{R} was impaired ($P<0.001$) over time in both UNCOMP and COMP, but was higher ($P<0.001$) throughout in UNCOMP (mean: COMP, $-131 \pm 14 \text{ W}/\text{m}^2$; UNCOMP, $+31 \pm 7 \text{ W}/\text{m}^2$). Similarly, \dot{E} heat loss increased ($P<0.001$) over time in both UNCOMP and COMP, but the extent was greater ($P<0.01$) throughout in UNCOMP (mean: COMP, $-236 \pm 22 \text{ W}/\text{m}^2$; UNCOMP, $-273 \pm 17 \text{ W}/\text{m}^2$). The rate of metabolic heat production was similar ($P>0.05$) through 15 min, after which it was lower ($P<0.05$) in UNCOMP (at 30 min: COMP, $+660 \pm 97 \text{ W}/\text{m}^2$; UNCOMP, $+524 \pm 98 \text{ W}/\text{m}^2$). Over time, \dot{M} was reduced ($P<0.05$) in UNCOMP from 20 min through completion but did not change ($P>0.05$) over time in COMP. Consequently, \dot{S} was higher ($P<0.01$) in UNCOMP through 25 min, but became similar ($P>0.05$) at 30 min (COMP, $+163 \pm 75 \text{ W}/\text{m}^2$; UNCOMP, $+196 \pm 82 \text{ W}/\text{m}^2$). Likewise, over time \dot{S} was reduced ($P<0.05$) in UNCOMP from 20 min through completion, but did not change ($P>0.05$) over time in COMP. Total body heat storage increased ($P<0.05$) over time in both UNCOMP and COMP, but was higher ($P<0.001$) in UNCOMP at all time points (at 30 min: COMP, $260 \pm 34 \text{ kJ}/\text{m}^2$; UNCOMP, $425 \pm 118 \text{ kJ}/\text{m}^2$). In UNCOMP power output and total body heat storage were found to be inversely correlated ($r = -0.994$; $P<0.001$), while no relationship between power output and total body heat storage was found in COMP ($r = 0.564$; $P>0.05$).

The HSI was lower ($P<0.01$) in COMP through 20 min, but was similar ($P>0.05$) to UNCOMP thereafter. The HSI, \dot{E}_{req} and \dot{E}_{max} over time in both COMP and UNCOMP

are presented in Figure 6.2 and Figure 6.3. Notably, HSI did not change ($P>0.05$) in COMP (starting HSI: 0.91 ± 0.19 , final HSI: 0.98 ± 0.21 ; Figure 6.2A), but improved ($P<0.05$) in UNCOMP (starting HSI: 1.21 ± 0.19 , final HSI: 0.97 ± 0.16 ; Figure 6.3A). This improvement in UNCOMP was due to a reduction ($P<0.01$) over time in \dot{E}_{req} (Figure 6.3B) and an increase ($P<0.01$) over time in \dot{E}_{max} (Figure 6.3C).

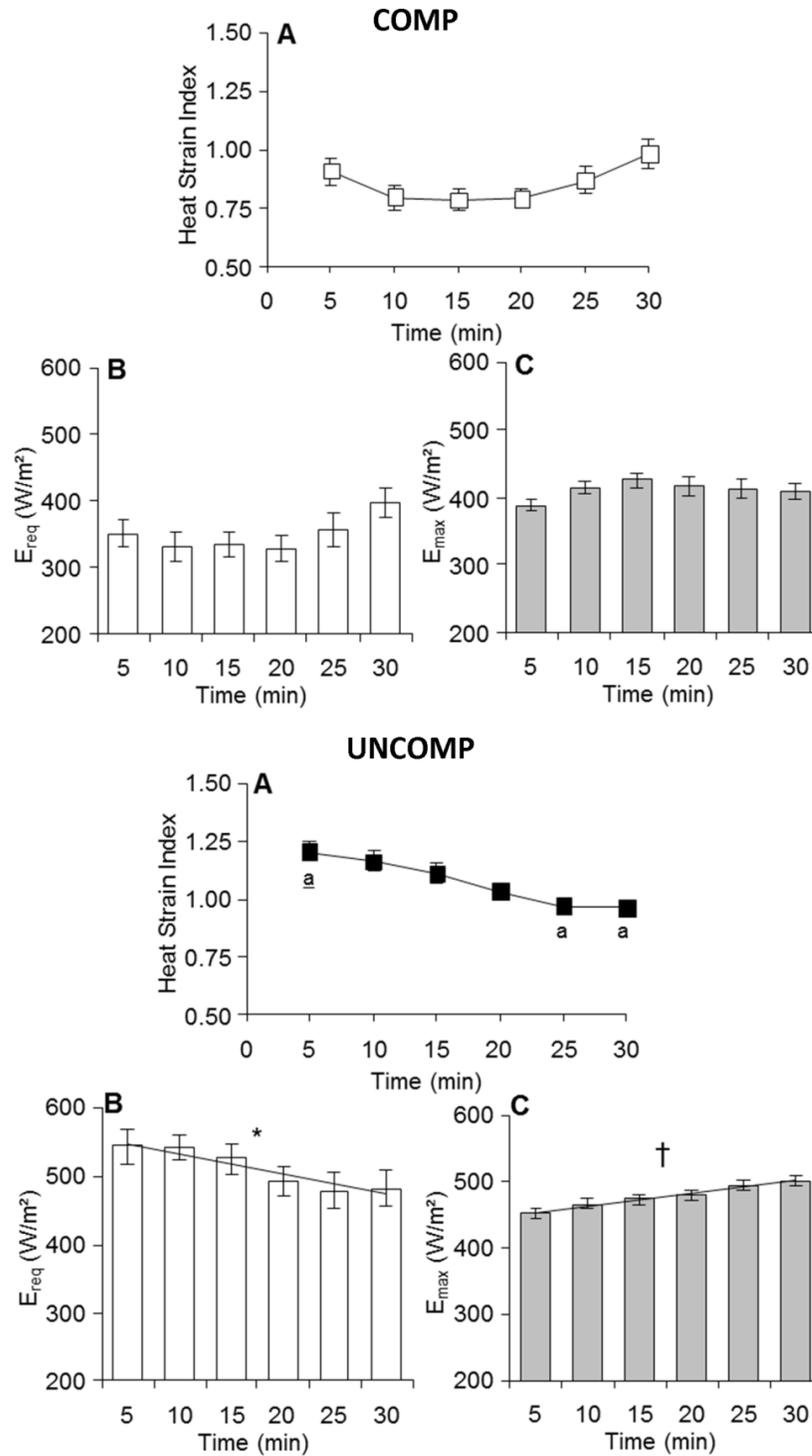


Figure 6.2: The time course of changes in the heat strain index (A), the required evaporation for heat balance (\dot{E}_{req} ; B), and the maximal evaporative capacity of the environment (\dot{E}_{max} ; C) during 30 min of self-paced exercise in a compensable (COMP) and an uncompensable (UNCOMP)

thermal environment (mean \pm SE). In COMP, there were no changes over time in the heat strain index, \dot{E}_{req} ($r = 0.636$, $P > 0.05$), or \dot{E}_{max} ($r = 0.636$, $P > 0.05$). In UNCOMP, * indicates a negative linear relationship (\dot{E}_{req} : $r = -0.955$, $P < 0.01$); † indicates a positive linear relationship (\dot{E}_{max} : $r = +0.991$, $P < 0.01$); letters indicate significant differences ($P < 0.05$) between underlined and the subsequent time points.

6.3.3: Perceptual Measures and Heart and Sweat Rate

Ratings of perceived exertion increased ($P < 0.01$) similarly ($P > 0.05$) over time in both trials (Figure 6.4A). Sensations of warmth and thermal discomfort increased ($P < 0.001$) in COMP and UNCOMP, but both warmth sensations and thermal discomfort (Figure 6.4B) were higher ($P < 0.001$) in UNCOMP throughout exercise. In UNCOMP, power output and thermal discomfort were found to be inversely correlated ($r = -0.953$; $P < 0.01$), while no relationship between power output and thermal discomfort was found in COMP ($r = 0.347$; $P > 0.05$). Heart rate increased ($P < 0.001$) similarly ($P > 0.05$) over time in both trials (heart rate at 5 min - UNCOMP: 159 ± 14 , COMP: 158 ± 13 ; at 30 min - UNCOMP: 178 ± 15 bpm, COMP: 178 ± 10 bpm). Whole body sweat rate was higher ($P < 0.001$) in UNCOMP (23.0 ± 6.7 g/min) than in COMP (16.1 ± 4.3 g/min).

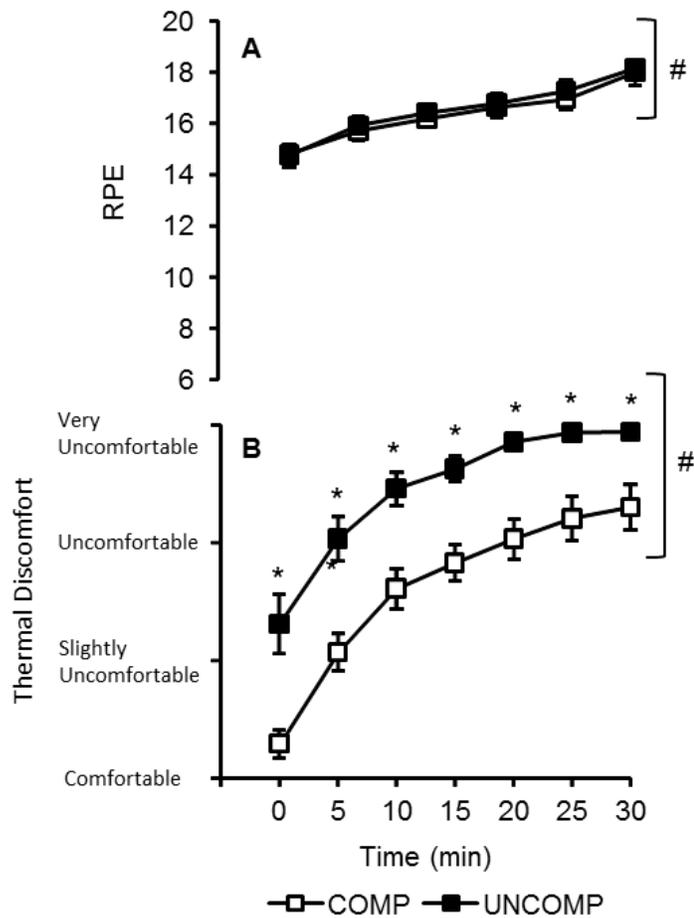


Figure 6.3: Ratings of perceived exertion (RPE; A) and thermal discomfort (B) during 30 min of self-paced exercise under uncompensable heat stress (UNCOMP) and in a compensable (COMP) thermal environment (mean \pm SE). * indicates significantly different than UNCOMP ($P < 0.01$); # indicates significant main effect of time ($P < 0.001$).

6.4: Discussion

The data presented have uniquely demonstrated that reductions in exercise intensity (Figure 6.1), and ultimately metabolic heat production, during self-paced exercise in the heat directly modify heat exchange over time (Figure 6.3B & Figure 6.3C), improving the compensability of the thermal environment (Figure 6.3A). Notably, no apparent relationships between exercise intensity (Figure 6.1) and the modification of heat exchange (Figure 6.2B, Figure 6.2C) and/or thermal compensability (Figure 6.2A) were

observed during self-paced exercise undertaken in a more moderate thermal environment. Thus, these data support the research hypothesis that voluntary reductions in exercise intensity in the heat are, by definition, thermoregulatory behaviors.

Cabanac (1996a) has implicitly stated that in order for a given behavior to be thermoregulatory in nature it must fulfill at least one of the following: a.) The response must be accompanied by a symmetrical response, i.e. if it occurs in the heat it must not occur in cooler conditions; b.) The response must be a quantitative function of ambient temperature and/or body temperatures; and c.) The response magnitude must be a function of the stimulus intensity. Furthermore, the IUPS Thermal Commission has defined thermal behavior as any coordinated movement establishing a more preferred condition for heat exchange between an organism and its environment (Mercer 2001). Additionally, it is also clear that thermal behavior strives to achieve and maintain heat balance (Romanovsky 2007; Schlader et al. 2009), and is initiated by a given level of (thermal) discomfort (Satinoff 1996). Thus, within the present investigation, it can be reasonably concluded that thermal behavior in the heat was observed because all of the following were satisfied: i.) Exercise intensity was consistently reduced (Figure 6.1); ii.) Heat exchange between the body and the environment improved over time, seemingly allowing for the attainment of heat balance (Figure 6.3); iii.) Changes in exercise intensity were associated with increases in thermal discomfort and total body heat storage; and iv.) There was no evidence for thermal behavior when self-paced exercise was undertaken in the more moderate condition (Figure 6.1, Figure 6.2).

As demonstrated (Figure 6.1), self-selected exercise intensity varies only slightly over time in a moderate environment (Ely et al. 2010; Tatterson et al. 2000; Tucker et al. 2004). Thus, the reductions in exercise intensity occurring in an uncompensably hot (Figure 6.1) environment observed in the present investigation, and previously (Ely et al. 2010; Tatterson et al. 2000; Tucker et al. 2004), are undoubtedly a quantitative function of ambient temperature. The consistency of these observations is portrayed by the findings that work completed (-75.1 ± 30.8 kJ), and therefore average exercise intensity (-47 ± 26 W), was reduced in all eleven subjects, by $21 \pm 5\%$. Additionally, the nature of

these responses has been further clarified via the unique observation that the reductions in exercise intensity occurring during self-paced exercise under uncompensable heat stress are, at least in part, governed by a conscious behavior. That is, self-selected ergometer load was lower from exercise commencement and reduced over time in the uncompensable condition (Figure 6.1B). Although the literature does not implicitly state that behavioral thermoregulation must be elicited by a conscious decision, thermal behavior is most likely initiated by the perception of discomfort (Satinoff 1996), and thus the decision to behaviorally thermoregulate is, at least partially, consciously derived. Furthermore, quantitative investigations into the control of human thermal behavior typically define this behavior in terms of a conscious response (e.g. Flouris and Cheung 2008; Schlader et al. 2009). By contrast, the self-paced exercise and heat stress literature is less clear (Flouris 2010), as it has been recently argued that exercise intensity is both subconsciously (Noakes et al. 2005; Tucker et al. 2004) and consciously (Maughan 2010) controlled. The data presented certainly indicate that there is a conscious element to this behavior (Figure 6.1B). However, it is recognized that a subconscious component to thermal behavior is also likely (e.g. as observed during sleep).

By placing subjects in a situation where heat exchange can be modified only by altering heat production (**Chapter Five**), this study was able to directly identify, presumably independent of autonomic temperature regulation, whether reducing exercise intensity in the heat aided heat exchange, and thus temperature regulation, over time. In accordance, thermal compensability was found to improve over time when exposed to uncompensable heat stress (Figure 6.3A), and this was, at least in part, due to a voluntary reduction in metabolic heat production. In fact, thermal compensability improved to such an extent that, in theory, heat balance could have been autonomically attained in the latter stages of exercise (Figure 6.3A). These alterations in thermal compensability were driven by the combination of an increase in the maximal evaporative capacity of the environment (Figure 6.3C) and a reduction in the evaporative requirement for heat balance (Figure 6.3B). Improvements in the maximal evaporative capacity of the environment were undoubtedly driven by the increase in skin temperature over time, which increased the water vapor pressure gradient between the skin and the surrounding environment, and

thus was not directly influenced by alterations in exercise intensity. By contrast, the reduction in the required evaporation was likely affected, to a certain extent, by the observed reductions in exercise intensity (Figure 6.1) and the corresponding rates and modes of heat exchange. Furthermore, reductions in exercise intensity were found to be associated with increases in total body heat storage ($r = -0.994$), while no apparent relationships over time were observed when exercise was undertaken in a thermally compensable environment (Figure 6.2).

Although correlation does not prove causation, the strong relationship between thermal discomfort and exercise intensity ($r = -0.953$) demonstrates similarities between the control of human thermoregulatory behavior at rest (e.g. Schlader et al. 2009) and the exercise intensity responses in the heat observed presently. Notably however, during exercise the role of thermal discomfort in behavior is less certain (Havenith et al. 2002). Therefore, during self-paced exercise the most dependable criterion measure dictating the selection of exercise intensity is likely that of perceived exertion (Tucker 2009). The purpose of this study was not to provide cause and effect and therefore a complete discussion of the potential control of this behavior is inappropriate. Nevertheless, it is notable that perceived exertion rose similarly in both trials (Figure 6.4A) despite differences in thermal discomfort (Figure 6.4B). This suggests that throughout exercise the subjects compared how they felt to how they expected themselves to feel at that moment and adjusted their exercise intensity appropriately (Joseph et al. 2008). Thus, it can be reasonably speculated that in the current paradigm elevations in ambient temperature challenged the control of the perception of effort and therefore exercise intensity was adjusted to protect this variable.

6.4.1: Considerations and Limitations

Currently there are several models attempting to explain the observed reductions in exercise intensity in the heat. These models include, but are certainly not limited to, centrally mediated anticipatory regulation (Marino 2004; Noakes et al. 2005), an increased cardiovascular strain and the associated reduction in relative oxygen uptake (Chevront et al. 2010), and a psychobiological model most recently described by

Marcora (2007; 2008). Notably however, both physiological and psychological factors probably play a large role in initiating this behavior (Cheung 2007b, 2010b). This investigation has described the thermal outcomes when the exerciser is given the freedom to choose exercise intensity during exposure to both an uncompensable and a compensable thermal environment. Therefore, these data are not intended to refute or support these models. However, considering the suggested role of the perception of effort in the control of this thermal behavior, any factors that affect the perception of effort will likely modify exercise intensity and the corresponding thermal outcomes. Consequently, it is likely that any (if not all) of the causal factors proposed in the abovementioned models may play a role in this behavior. Nevertheless, this certainly does not diminish the thermal behavioral evidence presented herein. Interestingly, this arrangement is seemingly mirrored by that of the many thermal and/or non-thermal modulators of several thermoregulatory responses (Mekjavic and Eiken 2006).

It is acknowledged that the partitioned calorimetric methods used to estimate body heat exchange are less sensitive than those of direct calorimetry. For instance, it is unlikely that the mean air velocity was constant over all of the body, while it is equally unlikely that P_{sk} will be saturated early during exercise. Fortunately, these data are not taken into account when calculating thermal compensability and therefore does not affect the conclusions of this study. Furthermore, it is also notable that human direct calorimetry facilities are rare. Estimates of mean skin temperature are improved by increasing skin temperature measurement locations (Mitchell and Wyndham 1969). It is therefore conceded that the four-site estimate of mean skin temperature used in these studies may be inaccurate. However, given that this subject cohort had a remarkably low percent body fat, that skin temperatures would not be considered 'cold' (Livingstone et al. 1987) and that thermal sensation mirrored changes in measured mean skin temperature, an inaccurate estimate appears unlikely. It is also recognized that a relatively slow changing core body temperature index was used in this study (Kolka et al. 1993). However, it is unlikely that measuring esophageal temperature, a faster changing index, would alter any conclusions made herein. For instance, within the present study differences in core temperature would have likely been observed earlier, but this would not have affected the

manner in which body heat exchange was estimated, and therefore would have little impact on the conclusions drawn.

6.4.2: Conclusions

This investigation has demonstrated that voluntary reductions in exercise intensity improves heat exchange over time, and therefore contributes to the regulation of body temperature. Thus, the data presented indicate that reductions in exercise intensity in the heat are, by definition, thermoregulatory behaviors. Given the difficulty in developing adequate models to evaluate the control of human thermoregulatory behavior, the enduring outcome of this investigation would be to use self-paced exercise in the heat as a model to evaluate this behavior.

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CHAPTER SEVEN

7.0: Skin Temperature as a Thermal Controller of Exercise Intensity

Publication(s) based on this chapter:

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Abstract

The present study examined the role of skin temperature on self-selected exercise intensity (power output). Eight well-trained, male cyclists completed two 60 min self-paced cycling bouts during which they completed as much work as possible. Using a liquid-perfused suit, skin temperature (\bar{T}_{Sk}) was changed ($P < 0.05$) during the two trials such that \bar{T}_{Sk} either started hot and was cooled (H to C) or started cold and was heated (C to H) throughout exercise. Pre-exercise core temperatures (T_C) and heart rates (HR) were similar ($P > 0.05$) between trials, while \bar{T}_{Sk} , thermal comfort and thermal sensation were higher ($P < 0.05$) in H to C. The change in T_{Sk} was similar ($P > 0.05$) in magnitude during the two trials (mean \pm SD; C to H: $-3.3 \pm 2.2^\circ\text{C}$; H to C: $+3.3 \pm 1.6^\circ\text{C}$). Work completed was greatest ($P < 0.01$) in C to H (C to H: 924.4 ± 139.1 kJ; H to C: 902.0 ± 127.1 kJ), which was attributed to a higher ($P < 0.05$) initial power output. T_C was similar ($P > 0.05$) between trials. HR was similar ($P > 0.05$) until 35 min had elapsed, after which it became lower ($P < 0.05$) in H to C. The perception of effort increased similarly ($P > 0.05$) between the two trials, while thermal comfort and thermal sensation generally reflected the changes observed in \bar{T}_{Sk} . These results indicate that upon exercise commencement T_{Sk} and the accompanying thermal perceptions are important inputs in the initial selection of exercise intensity.

Keywords

Temperature regulation, Exercise intensity, Metabolic heat production, Thermoregulatory behavior

7.1: Introduction

Behavior is generally considered to be the most effective (Parsons 2003) and limitless (Benzinger 1969) form of temperature regulation. Classic examples include, but are not limited to, adding or removing clothing, changing body positions, and adjusting the thermostat in a room. Notably, voluntary exercise is also a mode of thermoregulatory behavior (Mercer 2001), with voluntary muscular work in a cold environment resulting in the attainment of thermal comfort (Caputa and Cabanac 1980). However, rarely during exercise is producing enough heat a problem; more often it is the dissipation of this metabolic heat that challenges (temperature) regulation. Accordingly, self-paced exercise in the heat has been suggested as a model to evaluate thermoregulatory behavior (Budd 2001; Flouris 2010; Chapter 6; Morante and Brotherhood 2008) (**Chapter Six**). This model states that the compensability of the thermal environment can be manipulated by the exerciser through self-selected adjustments in the rate of metabolic heat production, i.e. exercise intensity (**Chapter Five** and **Chapter Six**). This behavior permits successful completion of the exercise task; however as a consequence, exercise performance in the heat is reduced relative to more moderate thermal conditions (Marino et al. 2004; Marino et al. 2000; Tatterson et al. 2000; Tucker et al. 2004).

Behavioral reductions in exercise intensity in the heat do not appear to be associated with increased levels of cardiovascular, thermoregulatory, or metabolic strain (Marino 2004). For instance, compared to exercise in a more moderate thermal environment, exercise intensity in the heat has been found to be reduced prior to any significant differences in heart rate, core temperature, or indicators of metabolism (Tatterson et al. 2000; Tucker et al. 2004). Accordingly, the signaling input(s) for these responses is not inherently clear, and therefore it is perhaps not surprising that this has been a recent topic of debate (Jay 2009; Jay and Kenny 2009; Marino et al. 2009; e.g. Tucker et al. 2006). Notably however, skin temperatures were consistently elevated throughout exercise (Tatterson et al. 2000; Tucker et al. 2004), and indeed high skin temperatures have been proposed as an important signaling input modulating exercise intensity (Jay 2009; Marcora 2007).

Elevated skin temperatures increase the perception of exercise effort at a given exercise intensity (Maw et al. 1993; Pivarnik et al. 1988), which is associated with increased skin blood flow (Rowell 1974) and sensations of warmth and thermal discomfort (Marcora 2007). Interestingly however, when exercise is self-paced the perceived exertion response appears to be preserved irrespective of attempts to disturb homeostasis (Tucker 2009). Therefore, in order to protect the perceived exertion response irrespective of ambient temperature in the heat a reduction in exercise intensity likely transpires. Accordingly, the perception of effort may be an important perceptual modulator of self-selected exercise intensity (Tucker 2009), with elevations in skin temperature, and associated physiological and perceptual responses, playing an integral role in the heat.

Indirectly, warm skin temperatures have been implicated as a thermal input explaining the observed reductions in exercise intensity during self-paced exercise in the heat (Jay 2009). However, the role of skin temperature in these responses has not been directly investigated. Therefore, the purpose of this study was to investigate the effect of skin temperature on self-selected exercise intensity. It was hypothesized that exercise intensity and skin temperature would be inversely related throughout exercise; i.e. high skin temperatures would elicit a reduction in exercise intensity, and this would result in a similar amount of work completed between experimental conditions. It was further hypothesized that the perceived exertion response would be defended in spite of changes in skin temperature, thermal comfort, and thermal sensation.

7.2: Methods

7.2.1: Experimental Overview

Eight male cyclists completed two 60 min self-paced cycling bouts during which they completed as much work as possible. Exercise intensity (power output) was freely adjustable and dependent upon cycling cadence. Throughout the two trials skin temperature either started cold and was heated or started hot and was cooled via a liquid conditioning garment (LCG). All trials took place at the same time of day and there were 7 days between each trial. The trials were conducted in a counter-balanced manner, minimizing any order effects.

7.2.2: Subjects

Eight healthy, well-trained male cyclists agreed to participate in the study. The subjects' characteristics were (mean \pm SD): age, 30 ± 9 y; height, 1.8 ± 0.1 m; weight, 71.8 ± 6.3 kg; body surface area, 1.90 ± 0.13 m²; maximal oxygen consumption ($\dot{V}O_{2\max}$), 5.07 ± 0.45 l/min; and percent body fat, $9.4 \pm 3.4\%$. Each subject was fully informed of the experimental procedures and possible risks before giving informed, written, consent. The protocol was approved by the University Human Ethics Committee and performed according to the Declaration of Helsinki. All subjects had participated in previous studies in our laboratory utilizing similar self-paced exercise protocols.

7.2.3: Preliminary Session

Approximately 1 week before the first experimental trial, subjects reported to the laboratory for anthropometric, submaximal and $\dot{V}O_{2\max}$ testing. These tests were conducted in a moderate environment ($20.3 \pm 1.5^{\circ}\text{C}$), with the exercise tests taking place on an electronically braked cycle ergometer (Lode Excalibur, Groningen, The Netherlands) set in the pedal rate independent (linear) mode. All subsequent exercise tests were completed on the same cycle ergometer. The tests first required the subjects to cycle for 6 min at each of four consecutive submaximal power outputs (100 W, 150 W, 200 W, and 250 W). Approximately five minutes after completion of the 250 W interval, during which time the subjects rested, an incremental exercise test (45 W/min) to volitional exhaustion was completed. A linear relationship between the mean rate of oxygen consumption during the last two minutes of each submaximal interval and power output was determined. This equation was used to calculate a workload which would elicit 80% of $\dot{V}O_{2\max}$ for each subject, and was later used to construct the self-paced exercise protocol.

7.2.4: Experimental Protocol

Approximately 6 days following the preliminary session, subjects arrived at the laboratory to participate in one of two experimental trials. These trials consisted of a 60 min bout of self-paced cycling exercise while wearing an LCG. During one of the trials the temperature of the liquid flowing through the LCG would start cold and would be

warmed during exercise such that the temperature of this liquid would be hot upon the completion of exercise (C to H). In the other trial the opposite occurred, the temperature of the liquid flowing through the LCG would start hot and would end cold. These two trials took place in the laboratory in similar ($P > 0.05$) moderate ambient conditions of: $18.3 \pm 1.5^{\circ}\text{C}$, $48.6 \pm 9.5\%$ relative humidity, and 20 km/h air speed. The subjects were blinded to the conditions as much as possible and were unaware of the research hypotheses, but due to changes in thermal sensation complete blinding was impossible. Thus, no attempt was made to deceive the subjects. It was assumed that the subjects were not heat acclimatized as the testing was conducted during the southern hemisphere winter/spring months (mean outdoor temperature: $12 \pm 4^{\circ}\text{C}$).

Pre-trial diet and hydration were controlled and confirmed as mentioned previously (*see Chapter Four*). Further activity and diet standardization was achieved via a standardized training ride 60 min in duration at a moderate intensity ($78 \pm 5\%$ heart rate max) the day before each trial (~24 h) and by the subjects consuming a standardized meal 3 h prior to the experimental trial. During all exercise bouts the subjects were required to drink 2 ml/kg of body weight of water every 15 min, which was maintained at the temperature of the laboratory.

On arrival at the laboratory, the subjects voided, and a nude body weight was obtained. A heart rate monitor and skin thermistors were then applied and this was followed by putting on the LCG. The subjects then rested, seated on the cycle ergometer for 15 min. This was followed by a capillary blood sample and a 5 min warm-up that transitioned into the 60 min self-paced cycling bout. When the exercise bout was complete another capillary blood sample was obtained, followed immediately by removal of the LCG, and a measurement of nude body weight. The duration of the procedures from initial to final nude body weight was ~90 min.

7.2.5: Experimental Procedures

7.2.5.1: Self-Paced Exercise

Following 15 min of rest, subjects completed a 5 min warm-up at 150 W which was followed by 60 min of self-paced cycling exercise that required the subjects to complete as great an amount of work as possible. Subjects were verbally encouraged every 5 min and were aware of elapsed time, but had no measure of work completed, cycling cadence, power output, or heart rate. Power output was proportionate to cycling cadence in a relationship defined by the linear factor. From the data collected during the preliminary session, this linear factor was calculated for each subject as follows: $LF = PO_{80\%} / (\text{rpm})^2$, where LF is the linear factor, $PO_{80\%}$ is the power output that would elicit 80% of $\dot{V}O_{2\text{max}}$, and rpm is the optimal cycling cadence chosen by each subject.

Immediately prior to commencement (i.e. post- warm-up), during, and upon completion of exercise, work completed, heart rate (HR), mean skin temperature (\bar{T}_{Sk}), core body temperature (T_{C}), thermal comfort, thermal sensation, and RPE were recorded every 5 min during exercise. Blood glucose and lactate were measured immediately prior to exercise commencement, at 30 min, and immediately upon completion. Plasma osmolality, percent changes in plasma volume, and whole body sweat rate were determined pre- to post-exercise. Power output was calculated from the work completed during every 5 min time period. Work completed was recorded from the cycle ergometer output.

7.2.5.2: Thermal Control

\bar{T}_{Sk} was manipulated using an LCG (CORETECH TUBEsuit, Delta Temax Inc., Pembroke, ON, Canada) that consisted of two pieces that covered the trunk, arms, and legs. Sewn inside this polyester/cotton garment was small polymer tubing. Liquid temperature was controlled (accurate to 0.1 °C) and pumped (flow rate: 1.9 L/min) using a liquid heater/cooler with a built-in pump (Grant Instruments Ltd., Cambridgeshire, UK). An additional cooling unit (Neslab Instruments Inc., Portsmouth NH, USA) was

used to supplement the aforementioned heater/cooler, helping to overcome the heat produced by the exercising subject that was transferred back to the liquid bath. The liquid pumped through the LCG was a mixture of water and anti-freeze. In order to maximize heat exchange between the LCG and the skin, subjects wore cycling shorts and no shirt under the LCG. Direct contact between the skin and the LCG was ensured at all times via the use of compression sleeves that were placed on the outside of the LCG over the arms and legs, and a compression vest that was placed over the trunk. To ensure a similar level of warm/cool sensation between trials subjects were instructed to maintain a similar posture throughout exercise during both trials.

At commencement of exercise, the temperature of the liquid flowing through the LCG was maintained at either $-6.6 \pm 1.5^{\circ}\text{C}$ (C to H) or $61.4 \pm 0.5^{\circ}\text{C}$ (H to C). The temperature of this liquid was maintained until 15 min of the exercise bout had elapsed. Between 15 min and 45 min the temperature of the liquid flowing through the LCG was warmed (C to H) or cooled (H to C) such that after 45 min had elapsed the temperature of the liquid was $61.2 \pm 0.6^{\circ}\text{C}$ (C to H) or $1.4 \pm 2.6^{\circ}\text{C}$ (H to C; Figure 7.1A). Throughout the experimental trials subjects gave no indication that these LCG liquid temperatures evoked cold or hot pain.

7.2.5.3: Measurements

Anthropometric characteristics, heart rate, \bar{T}_{sk} , RPE, thermal discomfort and thermal sensation were measured as described previously (*see Chapter Four*).

According to previously reported guidelines (Byrne and Lim 2007), subjects ingested a calibrated telemetric core body temperature sensor (CorTemp™, Palmetto FL, USA) 6 h prior to their experimental trial, which served as an indication of T_{C} .

Pre- to post-exercise nude body weight losses, corrected for fluid consumed, was used as an indicator of whole body sweat rate (e.g. Saunders et al. 2005).

Capillary blood lactate and glucose were assayed using a Lactate Pro (Mihami-Ku, Kyoto, Japan) and an Accu-Check Advantage glucose meter (Mannheim, Germany). Whole blood osmolality, hemoglobin and hematocrit were measured via an automated analyzer (ABL800 FLEX, Radiometer, Denmark), and percentage changes in plasma volume were calculated according to previously described methods (Dill and Costill 1974).

7.2.6: Statistical Analysis

All data were analyzed using a two-way (trial x time) repeated measures analysis of variance (ANOVA). Data were assessed for approximation to a normal distribution and sphericity, and no corrections were necessary. When the two-way ANOVA revealed an *F* test indicating a significant interaction or effect of time, *post hoc* pair-wise comparisons were made incorporating a Bonferroni adjustment. Additionally, paired *t*-tests were used where necessary in order to compare mean differences between trials.

According to the primary objective, the dynamics of the power output responses were further evaluated by log transforming both time (independent variable) and cumulative work completed (dependent variable) and analyzing the linear relationship ($y=y_0+a*x$; $P<0.001$; $R^2 = 1.00 \pm 0.00$) between the two variables for each subject. The mean *y*-intercept (*Y*₀) and slope (*a*) between the two conditions were compared via a paired *t*-test.

All data were analyzed using SPSS statistical software (V. 15, Chicago, IL, USA) with *a priori* statistical significance set at $P<0.05$. All data are reported as mean \pm SD unless otherwise noted.

7.3: Results

7.3.1: Thermal Control and Pre-Exercise

\bar{T}_{Sk} changed according to changes in bath temperature (Figure 7.1B). Notably, the change in \bar{T}_{Sk} was similar ($P>0.05$) in magnitude between C to H ($-3.3 \pm 2.2^{\circ}\text{C}$) and H to C ($+3.3$

$\pm 1.6^{\circ}\text{C}$). Furthermore, there was no difference ($P>0.05$) between the average mean skin temperatures throughout exercise in C to H ($31.3 \pm 1.2^{\circ}\text{C}$) and H to C ($31.9 \pm 1.2^{\circ}\text{C}$). The effects of the temperature of the liquid flowing through the LCG on the dependent variables immediately prior to exercise commencement (i.e. pre-exercise) are presented in Table 7.1.

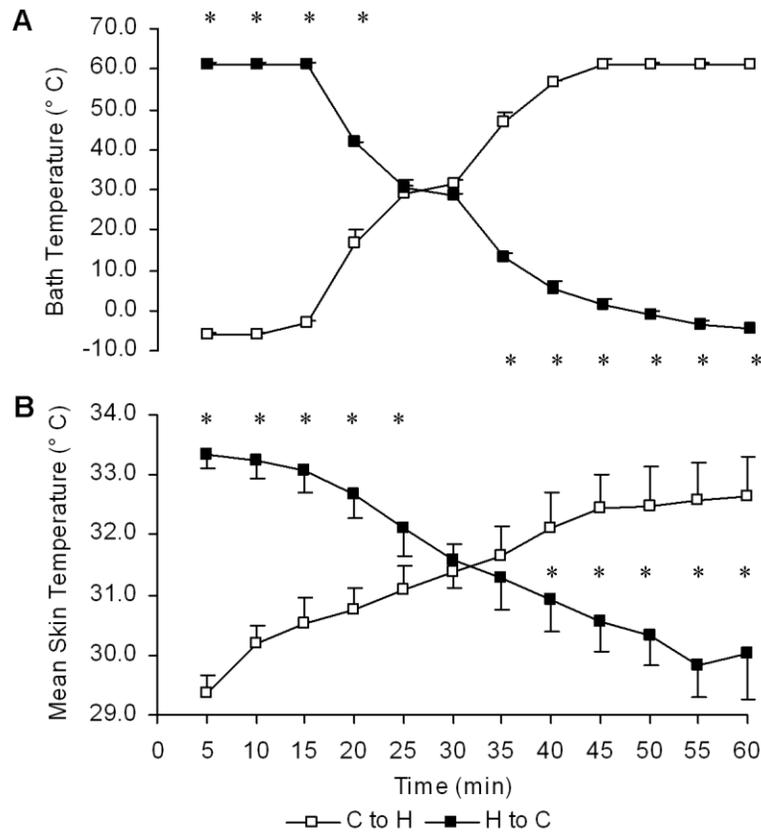


Figure 7.1: Temperature of the liquid in the bath (Bath Temperature) being pumped through the liquid conditioning garment (A) and mean skin temperature throughout the self-paced exercise tasks (mean \pm SE). * denotes significantly different than C to H ($P<0.05$).

Table 7.1: Pre-exercise variables (mean \pm SD)^a

	T _c (°C)	T _{sk} (°C)	Thermal Discomfort	Thermal Sensation	HR (bpm)
C to H	37.3 \pm 0.3	29.4 \pm 0.9	1.8 \pm 0.5	2.9 \pm 1.1	117 \pm 18
H to C	37.2 \pm 0.4	35.2 \pm 0.6 *	2.7 \pm 0.8 *	6.3 \pm 0.4 *	120 \pm 6

* Significantly different than C to H (P<0.05). ^a Post- warm-up, immediately prior to exercise commencement.

7.3.2: Exercise Intensity

The total amount of work completed (C to H: 924.4 \pm 139.1 kJ; H to C: 902.0 \pm 127.1 kJ), and therefore mean power output (C to H: 258 \pm 39 W; H to C: 251 \pm 35 W), was greater (P<0.01) in C to H than in H to C. This is attributed to a higher power output from the commencement of exercise in C to H (Figure 7.2) and is additionally described by a higher (P<0.05) y-intercept in C to H, yet similar (P>0.05) slope, in the log transformed work completed versus time linear regression model (Figure 7.3).

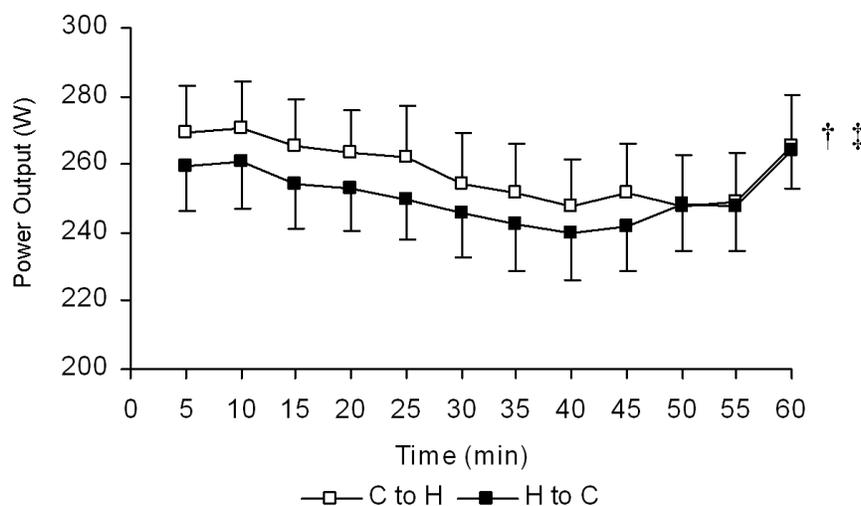


Figure 7.2: Power output during the self-paced exercise tasks (mean \pm SE). † denotes significant main effect of time (P<0.001); ‡ denotes significant main effect of trial (P<0.01).

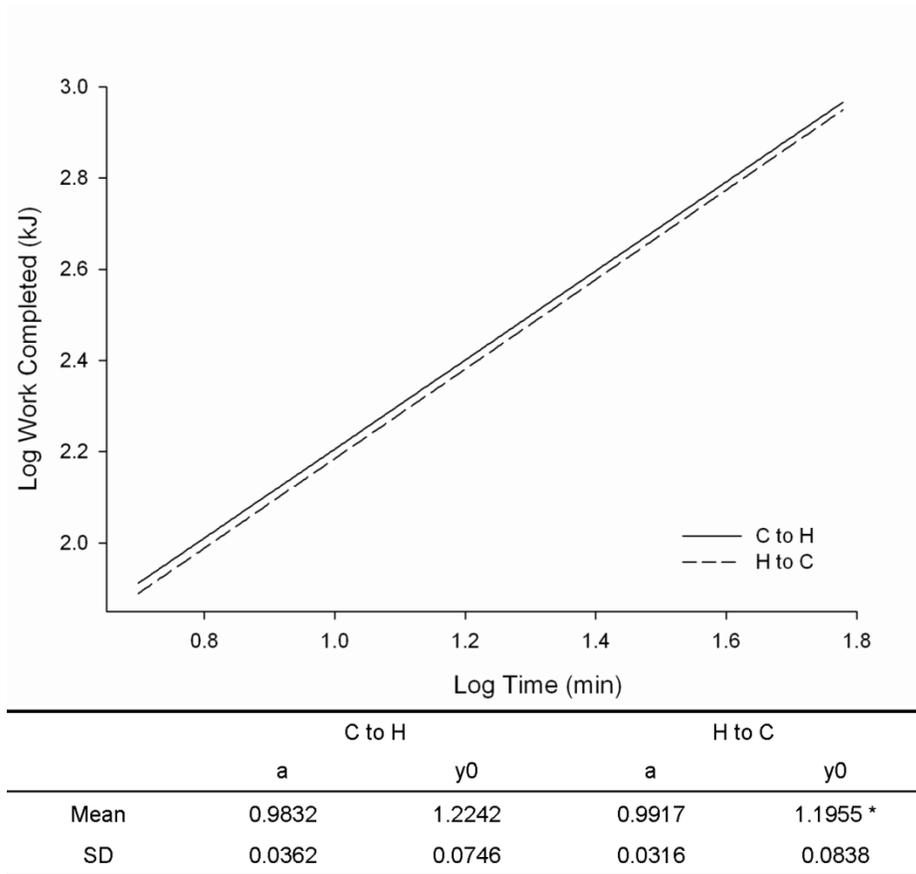


Figure 7.3: The graph is the mean log transformed linear regression model $[y=y_0+a*x]$ between time (min) and cumulative work completed (kJ) for both C to H and H to C. The table presents the mean linear regression model data, where ‘a’ is the slope of the linear regression line and ‘y0’ is the y-intercept. * denotes significantly different than C to H ($P<0.05$). These data indicate that power output started higher in C to H and that throughout the duration of exercise changes in power output were similar between the two trials.

7.3.3: Core Body Temperature, Heart Rate, and Perceptions

T_C rose ($P<0.001$) similarly ($P>0.05$) throughout exercise in both trials (Figure 7.4). HR was similar ($P>0.05$) between the two trials until 35 min had elapsed, after which HR was lower ($P<0.01$) in H to C (Figure 7.5). RPE increased ($P<0.001$) similarly ($P>0.05$)

between the two trials (Figure 7.6), while thermal comfort and thermal sensation generally reflected the changes observed in \bar{T}_{sk} (Figure 7.6B and Figure 7.6C).

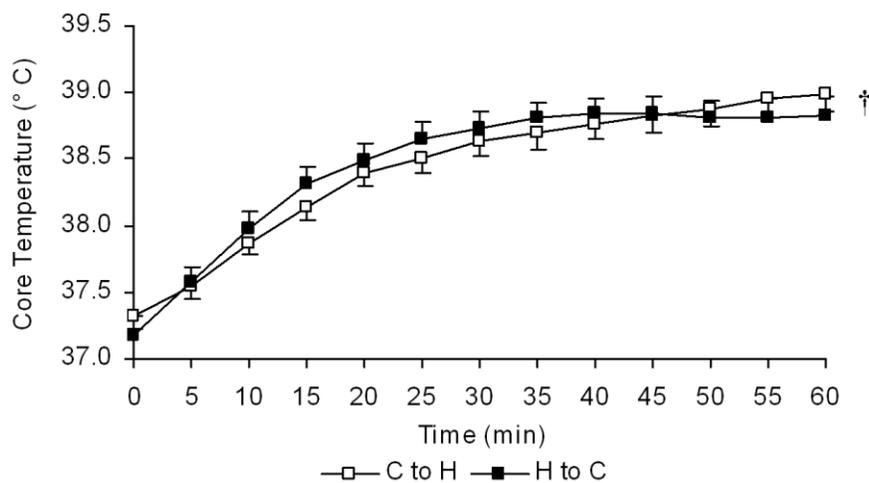


Figure 7.4: Core body temperature during the self-paced exercise tasks (mean \pm SE). † denotes significant main effect of time ($P < 0.001$).

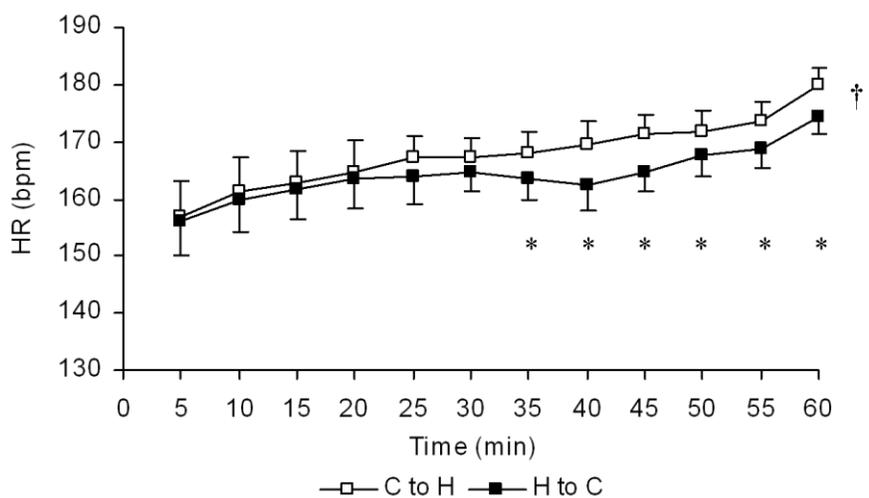


Figure 7.5: Heart rate (HR) during the self-paced exercise tasks (mean \pm SE).

† denotes significant main effect of time ($P < 0.001$); * denotes significantly different than C to H ($P < 0.05$).

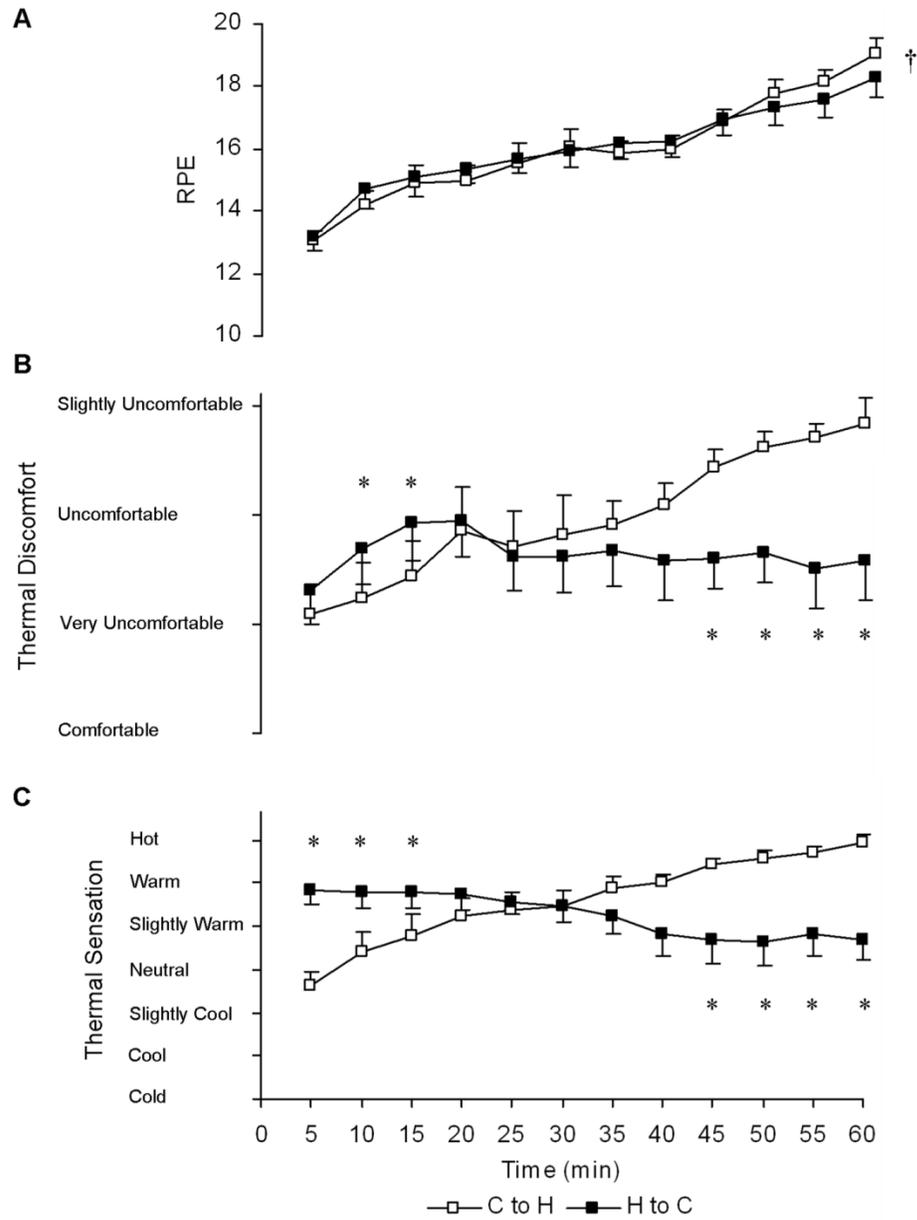


Figure 7.6: Ratings of perceived exertion (RPE; A), thermal discomfort (B) and thermal sensation (C) during the self-paced exercise tasks (mean \pm SE). † denotes significant main effect of time ($P < 0.001$); * denotes significantly different than C to H ($P < 0.05$).

7.3.4: Blood and Fluid Balance Indices

Blood glucose was similar between trials ($P>0.05$) and across time ($P>0.05$), while blood lactate increased ($P<0.001$) over time, but similarly ($P>0.05$) between trials. Whole body sweat rate was similar ($P>0.05$) between trials (H to C: 21.8 ± 3.3 g/min; C to H: 20.0 ± 6.6 g/min). Plasma osmolality rose significantly ($P<0.01$) in C to H (Pre - 281.6 ± 2.9 mOsm/kg H₂O; Post - 287.8 ± 4.5 mOsm/kg H₂O), yet was similar ($P>0.05$) in H to C (Pre - 282.6 ± 2.0 mOsm/kg H₂O; Post - 283.9 ± 1.8 mOsm/kg H₂O). The percentage change in plasma volume was similar ($P>0.05$) between the two trials (H to C: $-6.6 \pm 3.9\%$; C to H: $-6.7 \pm 4.8\%$).

7.4: Discussion

The purpose of the present study was to evaluate skin temperature as a thermal controller of exercise intensity. By utilizing an experimental methodology in which the temperature of the skin was either cooled or warmed during self-paced exercise we demonstrated that skin temperature plays an important role in the choice of exercise intensity upon exercise commencement. Interestingly, after the initial stages of exercise (i.e. >5 min), changes in skin temperature appear to play a less vital role. Additionally, the perception of effort response was found to be similar between trials irrespective of differences in exercise intensity, skin temperature, thermal comfort or thermal sensation, indicating that perceived exertion was behaviorally defended.

The data presented indicate that self-selected exercise intensity is strongly influenced by the thermal status of the body upon exercise commencement. Specifically, it has been demonstrated that skin temperature, and associated thermal perceptions (Table 7.1), are important in choosing the appropriate initial exercise intensity. Using self-paced exercise protocols in drastically different thermal environments, skin temperature has gained indirect support as a modulator of exercise intensity (Tatterson et al. 2000; Tucker et al. 2004), which suggests that skin temperature and exercise intensity would be inversely related – as hypothesized. The current data support this proposal only during the initial stages of exercise.

It was hypothesized that the total work completed in each trial would be similar, yet interestingly differences between trials were observed. This was found to be directly due to the chosen intensity at the onset of exercise (Figure 7.2 and Figure 7.3), which in the present paradigm was probably due to cooler skin temperatures. In hot and humid conditions, Kay et al. (1999) found a greater distance was completed during 30 min of self-paced cycling exercise when skin temperature was reduced upon exercise commencement. Unfortunately, exercise intensity (power output) was not reported at any time points, and accordingly the dynamics of this improvement were unknown. There is some evidence that chosen exercise intensity can be lower from the beginning of exercise in a hot environment, however in these instances elevated core temperatures accompanied the elevated skin temperatures (Marino et al. 2004; Marino et al. 2000). Therefore, until now the independent role of skin temperature on the dynamics of self-selected exercise intensity was unknown.

Elevations in skin temperature increase the perception of effort at a given exercise intensity (Maw et al. 1993; Pivarnik et al. 1988). During self-paced exercise however, the perception of effort response has been found to be both dependent (Tatterson et al. 2000) and independent (Tucker et al. 2004) of ambient/skin temperatures. The present study demonstrates that the perception of effort increased similarly throughout exercise in both experimental trials (Figure 7.6A) in spite of differences in skin temperature, exercise intensity, thermal comfort, thermal sensation, and heart rate. These data support the proposal that the perception of effort is a regulated perceptual variable and a controller of exercise intensity (Tucker 2009). Thus, the perception of effort response during self-paced exercise is regulated such that exercise intensity is controlled in order to protect the relationship between how subjects feel and how they expected to feel at that moment in time (Joseph et al. 2008). In the present paradigm, changing skin temperatures, and therefore thermal comfort and sensation, challenged the control of the perception of effort and therefore exercise intensity was adjusted in order to protect this variable. Interestingly however, this behavioral protection of the perception of effort response appears to be 'set' from the onset of exercise and does not appear to be affected by changes in skin temperature during the exercise bout.

Differences in skin temperature prior to (Table 7.1) and during (Figure 7.6B and Figure 7.6C) exercise resulted in modification of the perception of thermal comfort and thermal sensation. Since these factors possibly play a major role in determining a person's motivation to continue exercising in hot conditions (Cotter et al. 2001) thermal sensation and thermal comfort are likely perceptual modulators of exercise intensity (Marcora 2007). Interestingly, thermal perceptual changes during exercise (Figure 7.6B and Figure 7.6C) were not found to be associated with changes in exercise intensity (Figure 7.2 and Figure 7.3), demonstrating the importance of thermal sensation and thermal comfort at the onset of exercise (Table 7.1). Since perceptual factors are determined to a large extent by physiological changes (Cabanac 1971), it is difficult to elucidate any causal relationship between thermal perception and the self-selected exercise intensity. However, the controller(s) of exercise intensity under thermal stress are more than likely a combination of physiological and perceptual responses (Cheung 2007b).

7.4.1: Considerations and Limitations

It has been suggested that reductions in exercise intensity *during* self-paced exercise in the heat are thermoregulatory behaviors (Budd 2001; Morante and Brotherhood 2008). In the current study, it appears as though thermoregulatory behavior was elicited immediately upon exercise commencement, yet not dynamically during exercise. This suggests that the level of behavioral output (i.e. exercise intensity) was established at the start of exercise according to the predicted thermal consequences. Nevertheless, while the precise role of thermal behavior during exercise is not inherently clear, these findings corroborate previous work indicating that skin temperature is an important input in the control of thermoregulatory behavior in humans (Schlader et al. 2009).

This experimental protocol elicited a mean skin temperature difference of $\sim 5.8^{\circ}\text{C}$ upon exercise commencement (i.e. pre-exercise C to H: 29.4°C ; H to C: 35.2°C). At a core temperature of $\sim 37^{\circ}\text{C}$, a skin temperature of $\sim 29^{\circ}\text{C}$ would typically not be considered cool. Every effort was made in order to aid the liquid cooler. These provisions included adding another cooling unit and using an anti-freeze and water mixture, amongst others. However, these efforts were simply unable to overcome the significant heat produced by

the exercising subjects. This is a limitation that methodologically was unable to be overcome, yet the $\sim 5.8^{\circ}\text{C}$ skin temperature difference produced elicited interesting and meaningful results.

Given that intestinal temperature is slower to react to changes in body temperature than other indices of core temperature, e.g. esophageal temperature (Byrne and Lim 2007), it is acknowledged that the index of core temperature used may limit the conclusions herein. Notably however, intestinal temperature is faster to respond to changes in body temperature than rectal temperature (Byrne and Lim 2007), the preferred core temperature measurement location utilized in similar, relevant, studies (e.g. Gagge et al. 1969; Kay et al. 1999; Marino et al. 2004; Marino et al. 2000; Maw et al. 1993; Pivarnik et al. 1988; Saunders et al. 2005; Tatterson et al. 2000; Tucker et al. 2006; Tucker et al. 2004). Thus, it appears as though the measurement of intestinal temperature provides an advantage over rectal temperature, yet, not utilizing a faster responding index of core temperature perhaps limits our findings. Additionally, the measurement of mean skin temperature is improved with increasing the number of sites measured (Mitchell and Wyndham 1969), indicating that the skin temperature data presented may be inaccurate. However, given that the subjects utilized all had a similarly low percent body fat, that skin temperatures were not be considered ‘cold’ (Livingstone et al. 1987), and that thermal sensation coincided with changes in measured skin temperature (Figure 7.6C), it can be confidently stated that the four-site estimation of mean skin temperature adequately portrayed the effect that the temperature of the liquid flowing through the LCG had on skin temperature.

It was the intent of this study to directly evaluate the role of the temperature of the skin on self-selected exercise intensity, and this was achieved by conductive cooling/heating of the skin. When averaged across trials skin temperatures were similar, indicating that dry heat transfer was equivalent between trials. However, as a direct result of changing skin temperature and the metabolic heat produced during exercise, core-to-skin temperature gradients and the afferent inputs for autonomic thermoregulatory responses (e.g. skin blood flow and sweating) were undoubtedly altered throughout exercise.

Ultimately, this protocol tested the hypothesis that skin temperature modulates exercise intensity, but it would be naïve to ignore these potential physiological factors. For instance, changes in skin blood flow, and the accompanying cardiovascular responses, have been suggested to ultimately modulate exercise intensity (Cotter et al. 2001). Given the non-significantly higher heart rate at the onset of exercise (Table 7.1) these data do not necessarily refute this suggestion. However, it can be noted that dynamic cardiovascular changes during exercise (i.e. heart rate; Figure 7.5) did not affect exercise intensity (Figure 7.2 and Figure 7.3). While it is suggested that future studies evaluate these factors as potential modulators of exercise intensity, it is notable that these potentially confounding factors are unlikely to explain these observations. For example, changes in the physiological and heat exchange processes that occur with alterations in skin temperature would be expected to have larger effects later in exercise, rather than at the start, which was observed in the current study.

A 60 min exercise protocol was chosen as it mimicked previous tests conducted in this laboratory that all of the subjects had previously experienced. However, this may have limited the findings; perhaps using a relatively short exercise protocol unintentionally made the thermal status at the onset of exercise unnaturally important. Had the exercise bout continued beyond one hour, it is possible the inverse relationship between skin temperature and exercise intensity, evident during the initial stages of exercise, would have been observed during the latter stages of the exercise bout. This would be an important avenue for future research, but certainly does not diminish these findings.

7.4.2: Conclusions

Utilizing a unique experimental methodology in which the temperature of the skin was dynamically warmed and/or cooled during self-paced exercise, the present study demonstrates the important role of skin temperature in the thermal control of exercise intensity. Elevations in skin temperature, and probably any associated perceptions, e.g. thermal comfort and thermal sensation, prior to exercise commencement are largely responsible for the initial selection of exercise intensity. Interestingly however, skin temperature appears not to play a sustained role. Additionally, the regulation of the

perception of effort response may be the perceptual modulator of intensity during self-paced exercise.

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CHAPTER EIGHT

8.0: The Independent Roles of Temperature and Thermal Perception in the Control of Human Thermoregulatory Behavior

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Abstract

The present study independently evaluated temperature and thermal perception as controllers of thermoregulatory behavior in humans. This was accomplished using a self-paced exercise and heat stress model in which twelve physically active male subjects exercised at a constant subjective rating of perceived exertion (16, 'hard - very hard') while their face was thermally and non-thermally cooled, heated, or left alone (control trial). Thermal cooling and heating were achieved via forced convection, while non-thermal cooling and heating were accomplished via the topical application of menthol and capsaicin solutions. Evidence for thermoregulatory behavior was defined in terms of self-selected exercise intensity, and thus exercise work output. The results indicate that, in the absence of changes in temperature, non-thermal cooling and warming elicited thermal sensory and discomfort sensations similar to those observed during thermal cooling and warming. Furthermore, the perception of effort was maintained (mean \pm SD; 16.0 ± 0.1) throughout exercise in all trials. The initial (199 ± 40 W) and final (139 ± 28 W) exercise intensities were similar ($P > 0.05$), but exercise duration differed ($P < 0.05$) between conditions. Accordingly, thermal and non-thermal cooling resulted in the highest ($P < 0.05$) work output, while thermal warming the lowest ($P < 0.05$). Non-thermal warming and control trials were similar ($P > 0.05$). Heart rate, mean skin and core (rectal) temperatures, and whole body and local (neck) sweat rates were similar ($P > 0.05$) between all trials. These data indicate that changes in temperature are not a requirement for the initiation of thermoregulatory behavior in humans. Rather, thermal sensation and thermal discomfort are capable behavioral controllers.

Keywords

Exercise, Thermoregulation, Thermal discomfort, Menthol, Capsaicin, Thermal Sensation

8.1: Introduction

By definition, a thermoregulatory behavior establishes a preferred condition for heat exchange between an organism and its environment (Mercer 2001), thereby helping to ensure survival and optimize comfort (Parsons 2003). Compared to the relatively restricted capacity of autonomic thermoregulatory responses, behavioral responses are considered to be nearly limitless (Benzinger 1969) and are thus regarded as the ‘first line of defense’ in maintaining body temperatures (Werner et al. 2008).

Via their influence on thermal sensation (Mower 1976) and thermal discomfort (Cabanac 1971), both skin and core body temperatures are capable initiators of thermoregulatory behavior (Adair 1970; Cabanac et al. 1972; Cabanac et al. 1971; Carlisle 1968a; Flouris and Cheung 2008; Schlader et al. 2009; Stitt et al. 1971). However, when given behavioral freedom, core temperature changes too slowly for it to be the primary thermal signal (Weiss and Laties 1961), indicating that skin temperature is most likely the preferred behavioral input (Cabanac et al. 1971; Schlader et al. 2009). This arrangement effectively prevents unnecessary activation of water and/or energy consuming autonomic thermoregulatory responses (Romanovsky 2007), while suitably defending core body temperature (Schlader et al. 2009).

The voluntary control of exercise intensity (work output), and therefore metabolic heat production, when exposed to both cold and hot environments provides valuable insights into the control of human thermoregulatory behavior (Flouris 2010). For example, in the cold, thermal discomfort is improved by increases in exercise intensity (Cabanac and Leblanc 1983; Caputa and Cabanac 1980), while in the heat, voluntary reductions in work/exercise intensity effectively prevent body temperatures from rising excessively (Budd 2001; Morante and Brotherhood 2008). Thus, self-paced exercise under

environmental stress provides meaningful information concerning the control of thermoregulatory behavior in humans (Flouris 2010).

Given the causal relationships between body temperatures and the perception thereof, the fundamental mechanisms controlling human thermoregulatory behavior remain uncertain. For instance, skin temperatures, and the associated thermal perceptions, influence the voluntary selection of exercise intensity (**Chapter Seven**), but it is unclear as to whether a change in temperature must occur in order for this thermal behavior to be initiated. Indeed, it is highly possible that a change in thermal sensation, and thus discomfort, independent of changes in temperature is capable of commencing thermal behavioral responses.

Utilizing a self-paced exercise model, the purpose of this study was to independently evaluate temperature and thermal perception as controllers of human thermoregulatory behavior. Under heat stress, subjects were instructed to exercise at a constant (fixed) subjective rating of perceived exertion (e.g. Tucker et al. 2006) while their face was either thermally or non-thermally cooled, warmed, or left alone (control trial). Evidence for thermoregulatory behavior was defined in terms of self-selected exercise intensity, and thus total exercise work output, in a given trial. It was hypothesized that total work completed would be highest in both the thermal and non-thermal cooling trials, and lowest in the thermal and non-thermal heating trials. It was further hypothesized that these exercise responses would occur independent of differences in core body temperature, heart rate, or sweat rate.

Thermal cooling and heating were accomplished via forced convection, while non-thermal cooling and heating were achieved via the topical application of an 8.0% menthol gel and a 0.025% capsaicin cream. Acting mostly via the activation of the Transient Receptor Potential (TRP) ion channel Melastatin 8 (TRPM8) (Montell and Caterina 2007), during both rest (Green 1992; Hatem et al. 2006) and exercise (Gillis et al. 2010) menthol elicits a cooling sensation, thereby inhibiting the perception of warmth (Green 1986, 2005; Green 1992). Conversely, capsaicin, principally through the activation of the

TRP ion channel Vanilloid 1 (TRPV1) (Montell and Caterina 2007), elicits a warm, burning sensation (Green and Flammer 1988) thus enhancing sensations of warmth (Green 2005). The perceptual effects of both menthol and capsaicin transpire independent of changes in local (skin) temperature. Therefore, this paradigm permitted investigation into the distinct roles that both temperature and thermal perception may play in the control of human thermoregulatory behavior.

8.2: Methods

8.2.1: Experimental Overview

Twelve volunteers each completed five experimental trials in which they cycled at a constant (fixed) rating of perceived exertion (fixed-RPE) under significant heat stress. Exercise intensity (power output) was freely adjustable and dependent upon cycling cadence. During exercise, the face was either thermally or non-thermally cooled, warmed, or left alone (control trial). All trials took place at the same time of day and there were a minimum of 7 days between each trial. The trials were conducted in a randomized manner, to minimize any order effects.

8.2.2: Subjects

Twelve healthy, physically active males agreed to participate in the study. The subjects' characteristics were (mean \pm SD): age, 23 ± 5 y; height, 1.81 ± 0.10 m; weight, 84.0 ± 16.7 kg; body surface area, 2.04 ± 0.24 m²; and percent body fat, $11.7 \pm 5.1\%$. Each subject was fully informed of the experimental procedures and possible risks before giving informed, written, consent. Given that aerobically well-trained subjects have an altered perception of their physiological thermal strain during exercise (Tikusis et al. 2002), well-trained subjects were excluded. This also helped to reduce inter-subject variability. In the present study well-trained was defined in terms of the number of days per week a potential subject underwent aerobic exercise, and whether this exercise was recreational or more formal. All subjects who participated in this study exercised aerobically a maximum of 3 days per week, but were not taking part in any formal exercise training. This protocol was approved by the University Human Ethics Committee and performed according to the Declaration of Helsinki.

8.2.3: Preliminary Session

Seven days before the familiarization session, subjects reported to the laboratory for anthropometric measurements and an incremental exercise test. These tests were conducted in a moderate environment ($19.4 \pm 1.4^{\circ}\text{C}$), with the exercise tests taking place on an electronically braked cycle ergometer (Lode Excalibur, Groningen, The Netherlands) set in the pedal rate independent mode. All subsequent exercise tests were completed on the same cycle ergometer. The incremental exercise test started at a power output of 50 W for 3 min. Thereafter, power output increased by 50 W every 3 min until volitional exhaustion. This test was used to anchor the ‘high’ end (i.e. 19) of the rating of perceived exertion (RPE) scale (Noble and Robertson 1996). Five min following completion of the incremental exercise test, a power output and an optimal cadence that elicited an RPE of 16 was determined for each subject. This was later used to construct the fixed-RPE protocol. During these exercise tests power output, cadence, and elapsed time were blinded from the subjects.

8.2.4: Familiarization Session

Seven days following the preliminary session all subjects underwent a familiarization session. This session was conducted in a moderate environment ($20.7 \pm 3.5^{\circ}\text{C}$) and all experimental procedures were followed. This session fully familiarized the subjects with all experimental procedures and the fixed-RPE protocol.

8.2.5: Experimental Protocol

At least 7 days following the familiarization session, subjects arrived at the laboratory to participate in one of five experimental trials. During these trials the subjects were instructed to cycle at a fixed-RPE while wearing a hot liquid conditioning garment (LCG). During these trials the face was either thermally or non-thermally warmed, cooled, or left alone. Thermal cooling/warming was expected to elicit a change in both temperature and perception, while non-thermal cooling/warming was expected to elicit a change in thermal perception in the absence of a change in temperature. All experimental trials took place in the laboratory in similar ($P > 0.05$) moderate ambient conditions of: $20.3 \pm 0.5^{\circ}\text{C}$, $48 \pm 9\%$ relative humidity. No attempt was made to deceive the subjects,

but they were not informed of the experimental conditions and were kept unaware of the research hypotheses. However, due to changes in thermal sensation complete blinding was impossible. It was assumed that the subjects were not heat acclimatized as the testing was conducted during the southern hemisphere autumn/winter (mean outdoor temperature: $14.2 \pm 3.5^{\circ}\text{C}$).

Pre-trial diet and hydration were controlled and confirmed as mentioned previously (*see Chapter Four*). Subjects were not permitted to drink during any of the experimental procedures.

On arrival at the laboratory, the subjects voided, nude body weight was measured, and a rectal thermistor was self-inserted. A heart rate monitor, skin thermistors, and the ventilated capsule were then applied and this was followed by putting on the LCG. The subjects then rested, seated on the cycle ergometer for ~5 min. This was followed by a warm-up and the fixed-RPE protocol. When the exercise bout was complete the LCG and the remainder of the experimental equipment was promptly removed and nude body weight was measured.

8.2.6: Experimental Procedures

8.2.6.1: Fixed-RPE Protocol

Prior to commencing the fixed-RPE protocol, subjects completed a 10 min warm-up which required them to cycle for 4 min at an RPE of 11, 3 min at an RPE of 13, 2 min at an RPE of 15, and 1 min at an RPE of 17. This warm-up was modified from Lander *et al.* (2009) and was utilized to ensure the subjects were fully acquainted with the RPE scale prior to commencement of the fixed-RPE protocol.

Three min following completion of the warm-up, the fixed-RPE protocol commenced. This protocol required subjects to cycle at an RPE equal to 16 on the Borg ratings of perceived exertion scale (Borg 1970) and to adjust their power output accordingly. This rating lies between the verbal cues of ‘hard’ and ‘very hard.’ Prior to all preliminary,

familiarization, and experimental trials, the RPE scale was introduced and administered according to the recommendations set forth by Noble and Robertson (1996). The fixed-RPE protocol was performed as described previously (Tucker et al. 2006) and as follows: The power output measured during the first 3 min of each trial was averaged to calculate a starting mean power output. Subjects cycled until their power output fell to a value corresponding to 70% of the starting power output for 3 consecutive min. Formal instructions were orally presented to the subjects prior to the familiarization and each experimental session. Briefly, the subjects were instructed to exercise at power output that elicited an RPE of 16 and to change their power output accordingly. Furthermore, they were also made aware that the fixed-RPE protocol would be terminated following a sufficient reduction in power output, the magnitude of which was blinded to the subjects. Throughout exercise no feedback of work completed, power output, heart rate, cadence or time elapsed was provided to the subjects. At random intervals during exercise the subjects were verbally reminded by the researcher to maintain an RPE of 16. However, they were not verbally encouraged at any time. Power output was proportionate to cycling cadence in a relationship defined by the linear factor. From the data collected during the preliminary session, this linear factor was calculated for each subject as follows: $LF = PO_{RPE\ 16} / (rpm)^2$, where LF is the linear factor, $PO_{RPE\ 16}$ is the power output eliciting an RPE of 16, and rpm is the optimal cycling cadence chosen by each subject.

The fixed-RPE protocol was chosen given that RPE is a probable modulator of exercise intensity (Tucker 2009), and that skin (**Chapter Seven**) and ambient (Tucker et al. 2006) temperatures likely modify this response. Additionally, utilizing a protocol that does not evaluate performance *per se*, permitted the use of moderately active, rather than well-trained subjects, which was considered essential considering the perceptual factors mentioned previously (i.e. Tikuisis et al. 2002).

Immediately prior to commencement (i.e. post- warm-up), during, and upon completion of exercise, work completed, heart rate, mean skin temperature (\bar{T}_{sk}), core body temperature, and mean face temperature were recorded every minute, while RPE, local

sweat rate and whole body and face thermal discomfort and thermal sensation were recorded every 2 min. Whole body sweat rate was determined pre- to post-exercise. Power output was calculated from the work completed during every 1 min time interval.

8.2.6.2: Face Heating and Cooling

During the 3 min period between the warm-up and the fixed-RPE protocol, thermal or non-thermal face heating or cooling was initiated. The face was chosen as the site of experimental manipulation due to its small surface area (Brown and Williams 1982), the profound effect it has upon local and whole body thermal comfort (Cotter and Taylor 2005; Mundel et al. 2006a; Nakamura et al. 2008; Simmons et al. 2008), and its ability to modulate RPE at a given exercise intensity in the heat (Ansley et al. 2008; Armada-da-Silva et al. 2004; Mundel et al. 2007; Simmons et al. 2008).

Subjects' faces were thermally cooled (COOL) by a fan (Markec, Australia), located ~0.5 m from their face, which blew cool air (i.e. room air, ~20°C) at a speed of 0.74 m/s, while subjects' faces were thermally warmed (WARM) by a heater (EWT, Germany), located ~0.5 m from their face, which blew hot air (~45°C) at a speed of 0.29 m/s. Subjects were instructed to look directly into the fan/heater throughout these trials and this was enforced by the researcher. Facial heat loss and gain was estimated at -11.7 ± 1.7 W and $+4.1 \pm 0.7$ W for COOL and WARM. The magnitude of heat exchange was different ($P < 0.001$) between trials. During the control trial (CON) the face was left alone.

Subjects' faces were non-thermally cooled by applying an 8.0% menthol gel (Stopain, DRJ Group, Inc., USA) to the entire face in the dose of ~0.5 g per 100 cm² of skin (MEN), while subjects' faces were non-thermally warmed by applying a 0.025% capsaicin cream (Zostrix HP, AFT Pharmaceuticals Ltd., New Zealand) to the entire face in the dose of ~0.3 g per 100 cm² of skin (CAP). Pilot testing indicated that these concentrations of menthol and capsaicin elicited the desired perceptual effects, minimizing any side effects. Except for the menthol and capsaicin, the 8% menthol gel and the 0.025% capsaicin cream consisted of ingredients that are often considered physiologically and perceptually irrelevant. Notably, most of these other ingredients were

inert solvents, e.g. purified water, alcohols, etc. Both capsaicin and menthol were applied immediately post- warm-up following towel drying of sweat. There was no need to re-apply during exercise. Given the pungent smell associated with the menthol gel, during all experimental trials a gauze pad containing the menthol gel was placed near, but out of sight of, the subjects; this helped to blind the subjects from the experimental conditions. During all trials the subjects wore a pair of standard swimming goggles (Speedo, UK) to prevent eye irritation.

8.2.6.3: Thermal Control

Exogenous heat stress was applied via the use of an LCG (CORETECH TUBEsuit, Delta Temax Inc., Canada) that consisted of three pieces that covered the trunk, arms, and legs. Sewn inside this polyester/cotton garment is small polymer tubing. Liquid temperature was controlled (accurate to 0.1 °C) and pumped (flow rate: 15.7 L/min) using a water heater/cooler with a built-in pump (Neslab Instruments Inc. USA). Throughout all experimental trials $55.0 \pm 0.1^{\circ}\text{C}$ water was pumped through the LCG. In order to maximize heat exchange between the LCG and the skin, subjects wore only cycling/spandex shorts and no shirt under the LCG. Direct contact between the skin and the LCG was ensured at all times via the use of compression sleeves that were placed on the outside of the LCG over the arms and legs, and a compression vest that was placed over the trunk. To ensure a similar level of warmth between trials subjects maintained a similar posture during each trial. Subjects gave no indication that the LCG temperature evoked hot pain.

This modality of thermal control was chosen to prevent the unwanted perceptual effects of menthol and capsaicin that occur at high local (skin) temperatures. For instance, at high local temperatures menthol can elicit a burning sensation (Green 1992), that modulates sensations of warmth (Green 1985). Furthermore, high local temperatures also intensify the burning and stinging sensations associated with capsaicin (Green 2005). These unwanted side-effects could have drastically confounded the results had face temperatures been elevated, as would have occurred if exercise were undertaken in a hot ambient environment.

8.2.6.4: Measurements

Anthropometric characteristics, heart rate, \bar{T}_{sk} , RPE, thermal discomfort and thermal sensation were measured as described previously (*see Chapter Four*).

Rectal temperature served as an index of core body temperature, and was measured with a rectal thermistor (Mon-a-therm, Tyco Healthcare Group, USA) inserted 10 cm beyond the anal sphincter. Three skin thermistors were taped to the forehead and the right and left cheek using as little tape as possible. These temperatures were averaged (unweighted), giving an indication of mean face temperature.

Facial thermal discomfort and sensation were recorded via the same methods as whole body thermal discomfort and thermal sensation.

Local sweat rate was measured on the dorsal side of the neck via the ventilated capsule method (Graichen et al. 1982). Briefly, a capsule covering 3.5 cm² of skin was secured to the skin and was perfused with dry, compressed, air at a rate of 0.5 L/min. The effluent gas was sensed with humidity (Honeywell Ltd. New Zealand) and temperature (National Semiconductor, USA) probes located ~1 m away from the capsule. The neck was chosen as the measurement site as it was not under the direct influence of either face heating/cooling or the local warming effects of the LCG.

Pre- to post-exercise nude body weight losses were used as an indicator of whole body sweat rate. Given the variable nature of self-paced exercise a steady-state estimation of metabolic and respiratory fluid losses was not possible (e.g. Saunders et al. 2005).

8.2.7: Statistical Analysis

Total work, exercise time, the rate of power output decline, whole body sweat rate, and any pre-exercise (i.e. pre- warm-up) variables were analyzed using a one-way repeated measures analysis of variance (ANOVA). Due to between-subject variation, total work is presented relative to CON. The remainder of the dependent variables were analyzed using a two-way (trial x percent complete) ANOVA. Because trials varied in duration

these variables are expressed as a percentage of the total trial duration. All data were assessed for approximation to a normal distribution and sphericity, and when necessary degrees of freedom were adjusted using the Greenhouse-Geisser adjustment. When an ANOVA revealed a significant F test, Neuman-Kuels *post hoc* pair-wise comparisons were made. All data were analyzed using SPSS statistical software (V. 15, Chicago, IL, USA) with *a priori* statistical significance set at $P < 0.05$. All data are reported as mean \pm SD unless otherwise noted.

8.3: Results

RPE was similarly ($P > 0.05$) maintained in all trials (overall mean RPE: 16.0 ± 0.1).

8.3.1: Thermal Behavior

Total work completed, as a percentage relative to CON, is presented in Figure 8.1. Total work completed differed ($P < 0.01$) amongst trials (CON: 189.4 ± 58.0 kJ; COOL: 223.2 ± 73.0 kJ; WARM: 160.0 ± 48.2 kJ; MEN: 228.7 ± 82.1 kJ; CAP: 178.8 ± 60.6 kJ). Mean power output responses during the first 3 min and final 3 min of exercise were similar ($P > 0.05$) in all trials, and are presented, relative to actual time, in Figure 8.2A. Given that starting mean power outputs (mean: 199 ± 40 W) were similar ($P > 0.05$) between trials (Figure 8.2A), the fixed-RPE protocol was ceased at similar power outputs irrespective of trial (mean 70% of starting power output: 139 ± 28 W; Figure 8.2A). The rate of power output decline differed ($P < 0.01$) among trials and is presented in Figure 8.2B.

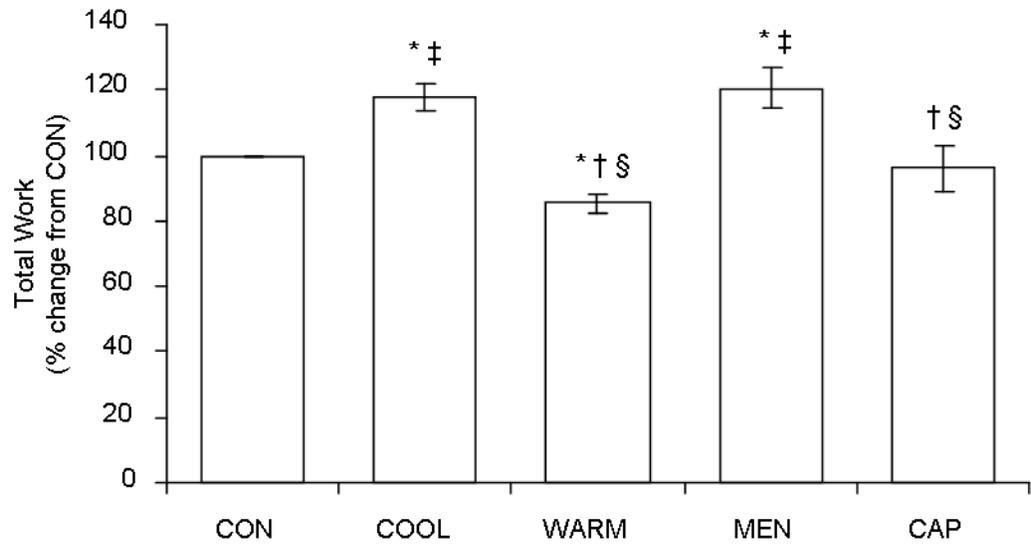


Figure 8.1: Total work completed expressed as a percentage relative to CON (mean \pm SE). * denotes significantly different than CON ($P < 0.05$); † denotes significantly different than COOL ($P < 0.05$); ‡ denotes significantly different than WARM ($P < 0.05$); § denotes significantly different than MEN ($P < 0.05$).

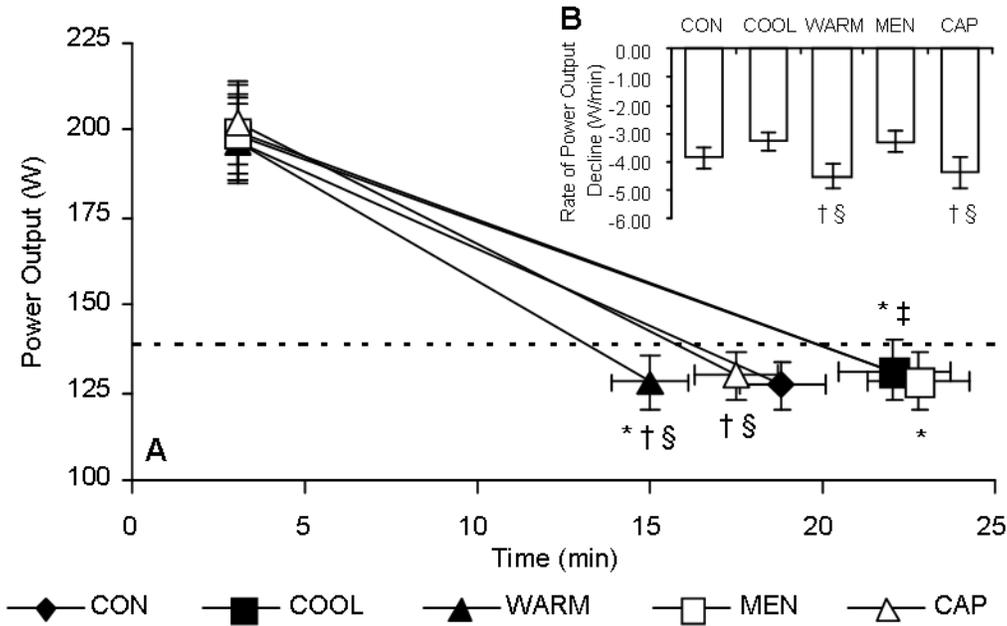


Figure 8.2: Mean power output responses during the first 3 min and final 3 min of exercise expressed relative to actual time (A), and the rate of power output decline (B; mean \pm SE). Dashed line indicates 70% of starting power output (mean: 139 ± 28 W). With respect to time (x-axis): * denotes significantly different than CON ($P < 0.05$); † denotes significantly different than COOL ($P < 0.05$); ‡ denotes significantly different than WARM ($P < 0.05$); § denotes significantly different than MEN ($P < 0.05$).

8.3.2: Body Temperatures and Thermal Perceptions

Pre-exercise (i.e. pre- warm-up) core body temperatures were similar between all trials ($P > 0.05$; CON: $36.9 \pm 0.4^\circ\text{C}$; COOL: $36.9 \pm 0.3^\circ\text{C}$; WARM: $36.9 \pm 0.4^\circ\text{C}$; MEN: $36.8 \pm 0.3^\circ\text{C}$; CAP: $37.0 \pm 0.5^\circ\text{C}$). The change in core body temperature from exercise commencement was different ($P < 0.05$) between MEN and WARM, yet was similar ($P > 0.05$) between all other trials (CON: $0.74 \pm 0.22^\circ\text{C}$; COOL: $0.84 \pm 0.38^\circ\text{C}$; WARM: $0.68 \pm 0.31^\circ\text{C}$; MEN: $0.97 \pm 0.46^\circ\text{C}$; CAP: $0.81 \pm 0.41^\circ\text{C}$). The rate of rise in core body temperature was similar ($P > 0.05$) amongst all trials (CON: $0.0403 \pm 0.0144^\circ\text{C}/\text{min}$; COOL: $0.0386 \pm 0.0171^\circ\text{C}/\text{min}$; WARM: $0.0450 \pm 0.0239^\circ\text{C}/\text{min}$; MEN: $0.0460 \pm 0.0219^\circ\text{C}/\text{min}$; CAP: $0.0467 \pm 0.0198^\circ\text{C}/\text{min}$). Mean skin temperatures were similar ($P > 0.05$) between all trials (CON: $36.5 \pm 0.7^\circ\text{C}$; COOL: $36.3 \pm 0.8^\circ\text{C}$; WARM:

$36.8 \pm 0.5^{\circ}\text{C}$; MEN: $36.6 \pm 0.9^{\circ}\text{C}$; CAP: $36.6 \pm 0.8^{\circ}\text{C}$). Mean face temperatures during CON, CAP, and MEN were similar ($P>0.05$), yet were warmer ($P<0.001$) and cooler ($P<0.001$) than COOL and WARM (CON: $35.0 \pm 0.8^{\circ}\text{C}$; COOL: $31.8 \pm 1.8^{\circ}\text{C}$; WARM: $38.4 \pm 1.2^{\circ}\text{C}$; MEN: $35.1 \pm 0.8^{\circ}\text{C}$; CAP: $35.4 \pm 0.8^{\circ}\text{C}$). Core body, mean skin, and mean face temperatures, expressed relative to the percentage of total time, are presented in Figure 8.3. Facial and whole body thermal discomfort and sensation were modulated ($P<0.001$) by trial and are presented in Figure 8.4 and Figure 8.5.

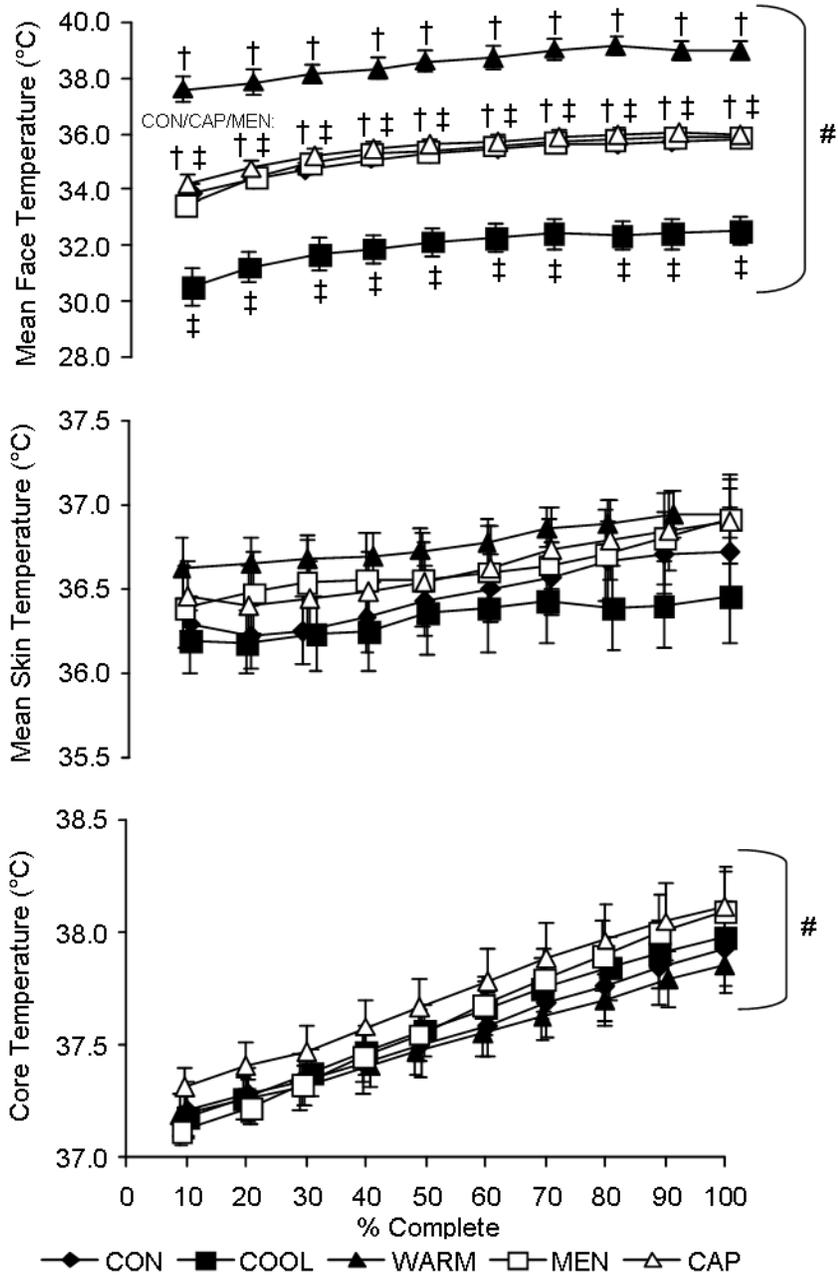


Figure 8.3: Mean face (A), mean skin (B), and core (C) body temperatures expressed as a percentage relative to the total trial duration (mean \pm SE). † denotes significantly different than COOL ($P < 0.05$); ‡ denotes significantly different than WARM ($P < 0.05$); # denotes significant main effect of time ($P < 0.001$).

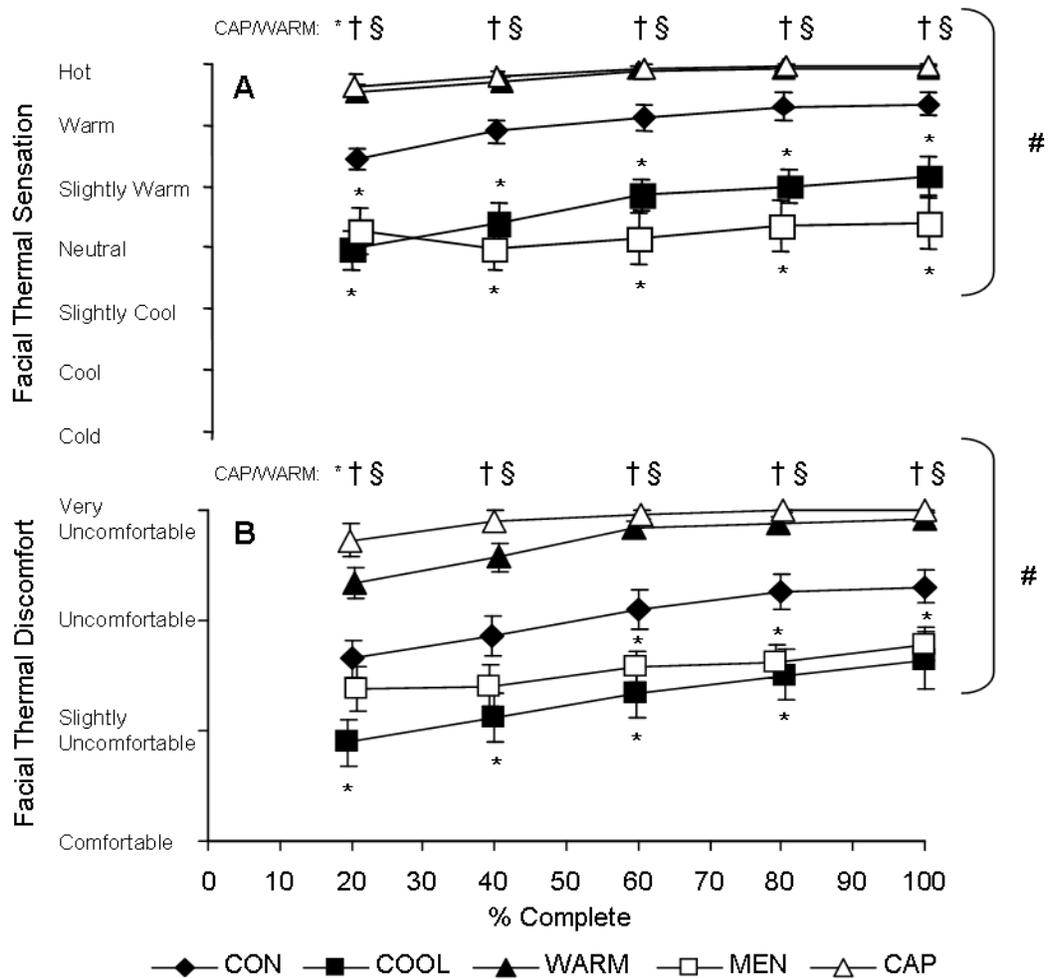


Figure 8.4: Facial thermal sensation (A) and thermal discomfort (B) expressed as a percentage relative to the total trial duration (mean \pm SE). * denotes significantly different than CON ($P < 0.05$); † denotes significantly different than COOL ($P < 0.05$); § denotes significantly different than MEN ($P < 0.05$); # denotes significant main effect of time ($P < 0.001$).

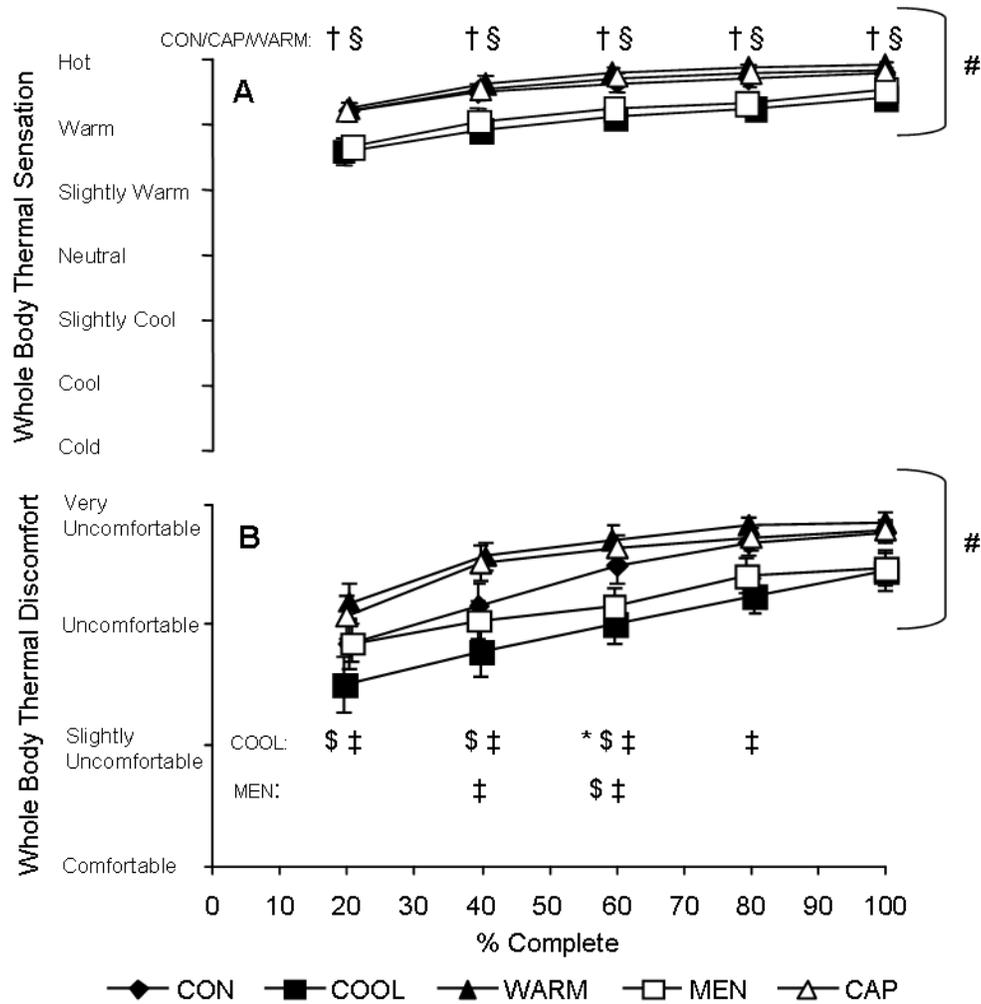


Figure 8.5: Whole body thermal sensation (A) and thermal discomfort (B) expressed as a percentage relative to the total trial duration (mean \pm SE). * denotes significantly different than CON ($P < 0.05$); † denotes significantly different than COOL ($P < 0.05$); § denotes significantly different than MEN ($P < 0.05$); \$ denotes significantly different than CAP ($P < 0.05$); ‡ denotes significantly different than WARM ($P < 0.05$); # denotes significant main effect of time ($P < 0.001$).

8.3.3: Heart and Sweat Rates

Pre-exercise (i.e. pre- warm-up) heart rates were similar ($P > 0.05$; CON: 73 ± 9 bpm; COOL: 77 ± 9 bpm; WARM: 79 ± 11 bpm; MEN: 74 ± 11 bpm; CAP: 77 ± 8 bpm). During exercise, heart rates changed ($P < 0.05$) similarly ($P > 0.05$) over time in all trials

(mean heart rate during the first 3 min (bpm), mean heart rate during the final 3 min (bpm); CON: 156 ± 10 bpm, 161 ± 15 bpm; COOL: 153 ± 10 bpm, 156 ± 15 bpm; WARM: 159 ± 14 bpm, 163 ± 16 bpm; MEN: 153 ± 10 bpm, 163 ± 11 bpm; CAP: 156 ± 12 bpm, 160 ± 19 bpm). Heart rate throughout all trials, expressed relative to the percentage of total time, is presented in Figure 8.6. Whole body sweat rate was similar ($P > 0.05$) between trials (CON, 24.2 ± 7.7 g/min; COOL, 25.5 ± 5.4 g/min; WARM, 28.9 ± 8.8 g/min; MEN, 23.7 ± 7.0 g/min; CAP, 26.6 ± 6.6 g/min). Local sweat rate, expressed relative to the percentage of total time, is presented in Figure 8.7.

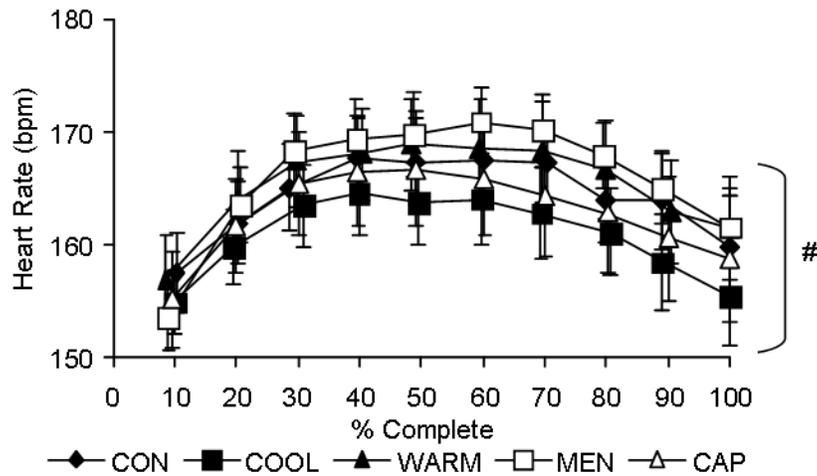


Figure 8.6: Heart rate expressed as a percentage relative to the total trial duration (mean \pm SE). # denotes significant main effect of time ($P < 0.001$).

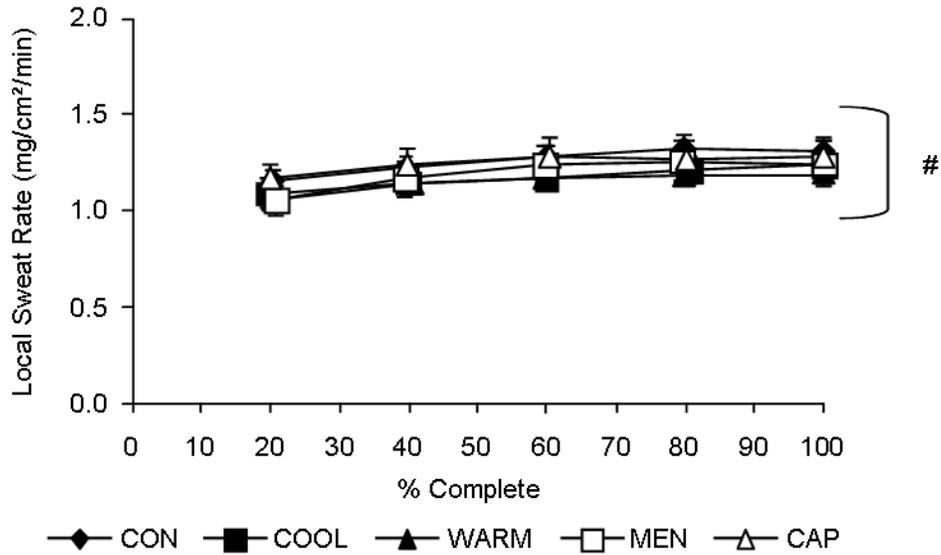


Figure 8.7: Local sweat rate, on the dorsal of the neck, expressed as a percentage relative to the total trial duration (mean \pm SE). # denotes significant main effect of time ($P < 0.001$).

8.4: Discussion

The present study utilized a novel self-paced exercise and heat stress model to evaluate temperature and thermal perception as distinct controllers of human thermoregulatory behavior. In this paradigm the face was thermally and non-thermally cooled, heated, or left alone while exercise intensity was voluntarily selected in order to maintain a constant subjective rating of perceived exertion. The results demonstrate that both (facial) temperature and thermal perception are capable modulators of exercise work output. Thus, it has been uniquely shown that a physical (thermal) change in temperature is not a necessary requirement for the initiation of thermoregulatory behavior in humans.

Although it comprises only ~8-10% of the total body surface area (Brown and Williams 1982), under heat stress the temperature of the face has a profound effect upon local and whole body thermal discomfort (Cotter and Taylor 2005; Mundel et al. 2006a; Nakamura et al. 2008; Simmons et al. 2008). Via face cooling during exercise in the heat, these effects are manifested in a reduced perception of effort at a given intensity (Ansley et al. 2008; Armada-da-Silva et al. 2004; Mundel et al. 2007; Simmons et al. 2008). Until

now, the only behavioral outcome related to these perceptual responses to face cooling during exercise in the heat, has been a longer time to volitional exhaustion (Ansley et al. 2008). It was observed that thermal face cooling (Figure 8.3A) affected both facial (Figure 8.4) and whole body (Figure 8.5) perceptual responses by inhibiting sensations of warmth and decreasing thermal discomfort. However, in the current model, this was translated into a longer exercise duration (Figure 8.2), and therefore higher exercise work output (Figure 8.1). Conversely, thermal face heating (Figure 8.3A) increased facial (Figure 8.4) and whole body (Figure 8.5) sensations of warmth and thermal discomfort, which resulted in a reduction in exercise duration (Figure 8.2A) and the lowest exercise work output (Figure 8.1). The modulating capabilities of both thermal face cooling and heating on self-selected exercise intensity responses is unique. Furthermore, it is interesting that the extent of estimated heat loss/gain resulting from facial cooling and warming was different, yet exercise time relative to the control trial was nearly identical in magnitude (~3 min). This supports the contention that the sensitivity of the initiation of thermal behavior in humans is modified by the extent of skin cooling/heating (i.e. heat loss/gain) (Schlader et al. 2009) (**Chapter Seven**). Most importantly however, these data indicate that under heat stress, facial temperature is capable of modulating behavioral responses bi-directionally; i.e. both positively (thermal cooling) and negatively (thermal warming).

In order to discern the independent effects of (facial) temperature and thermal perception on self-selected exercise responses, this study intended to effectively mimic the perceptual effects of thermal cooling and warming in the absence of a change in temperature. This non-thermal cooling and warming was accomplished by topically applying a menthol gel and a capsaicin cream to the face immediately prior to exercise commencement. These efforts were seemingly successful (Figure 8.3A & Figure 8.4).

The topical application of an 8.0% menthol gel to the face inhibited the perception of warmth (Figure 8.4) independent of reductions in face temperature (Figure 8.3A). While this translated into cooler whole body thermal sensations (Figure 8.5A), it is interesting that whole body thermal discomfort was not as dramatically improved as observed during

face cooling (Figure 8.5B). Similar to the findings presented, during both rest (Green 1992; Hatem et al. 2006) and exercise (Gillis et al. 2010), the cutaneous application of menthol has been previously shown to elicit a cooling sensation, inhibiting perceptions of warmth (Green 1986, 2005; Green 1992). In the present study, it has been demonstrated that these perceptual outcomes can be transformed into responses similar to those occurring during thermal cooling (Figure 8.1 & Figure 8.2). Given that the menthol receptor, TRPM8, is important in detecting and adequately responding to cold ambient conditions (Bautista et al. 2007; Dhaka et al. 2002), these similarities were not unexpected. Parallel to the current findings, topical menthol application has been found previously to induce heat seeking behavior in mice (Tajino et al. 2007), similar to what would be expected during cold exposure. In addition to its sensory (and behavioral) effects, the topical application of menthol disturbs the sweating response to exercise (Kounalakis et al. 2010), generally promoting heat-gain responses (Tajino et al. 2007). In the present study any potential effect of these responses was likely reduced by applying the menthol gel to the face, a small surface area (Brown and Williams 1982). Importantly, both whole body and local (neck) sweat rates (Figure 8.7), indicators of the rate of evaporative heat loss, were unaffected by menthol.

In agreement with previous findings (Green 2005), the topical application of a 0.025% capsaicin cream to the face elicited both facial (Figure 8.4) and whole body (Figure 8.5), sensations of warmth and thermal discomfort in the absence of increases in facial temperature (Figure 8.3A). Interestingly, the behavioral responses observed did not mimic those of thermal face heating (Figure 8.1 & Figure 8.2). Although capsaicin is associated with burning and stinging sensations (Green and Flammer 1988), the present study attempted to minimize them by utilizing an LCG to promote heat stress. Nevertheless, given that the capsaicin receptor, TRPV1, is activated by noxious heat (Caterina et al. 1999; Caterina et al. 1997) and is causally associated with thermal nociception and pain sensation (Caterina et al. 2000) but is not associated with innocuous thermal sensation or thermoregulatory behavior (Moqrich et al. 2005; Shimizu et al. 2005), it is likely that capsaicin elicited thermal pain, but not necessarily thermal discomfort. Although the precise role of TRPV1, and thus capsaicin, in temperature

regulation remains equivocal (Gavva 2008; Romanovsky et al. 2009), the topical application of capsaicin augments cutaneous vasodilation in humans (Stephens et al. 2001), suggesting that TRPV1 may indeed play a thermoregulatory role. Nevertheless, despite sensations of warmth and thermal discomfort, given its nociceptive nature the current paradigm was simply not able to adequately test the research hypotheses using capsaicin. It is suggested that future investigations target the TRP ion channel Vanilloid 3 (TRPV3), which appears to be involved in warm (innocuous) thermal sensation and behavior, and is non-thermally activated by camphor (Moqrich et al. 2005).

8.4.1: Considerations and Limitations

Both core and skin temperatures are established controllers of thermal behavioral responses in humans during both rest (Cabanac et al. 1972; Cabanac et al. 1971; Flouris and Cheung 2008; Schlader et al. 2009) and exercise (Marino et al. 2004) (**Chapter Seven**). However, prior to discernable changes in core body temperature, skin temperature is a more than capable controller (Cabanac et al. 1971; Schlader et al. 2009) (**Chapter Seven**). Given that this study aimed to only examine changes in skin temperature and thermal perception as controllers of this behavior, any differences in core body temperature would have likely confounded the results. Hence, it is notable that the core body (rectal) temperature responses were similar amongst all trials (Figure 8.3C). However, it is recognized that the core temperature measurement location (the rectum) is a relatively slow changing core body temperature index (Byrne and Lim 2007). This potential short coming precludes the exclusion of core temperature as a potential controlling factor of thermal behavior in the present paradigm. Another notable methodological limitation is the four-site estimate of mean skin temperature utilized in this study. Estimates of mean skin temperature are improved by increasing skin temperature measurement locations (Mitchell and Wyndham 1969), therefore this estimate may be inaccurate. However, given that similarly hot water was pumped through the LCG in all trials, the relatively low percent body fat of the subjects and that skin temperatures would be considered ‘hot’ (Livingstone et al. 1987), it can be confidently stated that the four-site estimate of mean skin temperature adequately portrayed the ‘clamping’ effect of the LCG on skin temperature. Thermal aspects aside,

other potentially confounding factors were also seemingly accounted for. For instance, cardiovascular factors have been suggested to influence self-selected exercise intensity in the heat (Cheuvront et al. 2010; Cotter et al. 2001), while skin wettedness influences local and whole body thermal discomfort (Fukazawa and Havenith 2009). Notably, the thermal behavioral responses observed in the current study appear to occur independent of differences in heart rate (Figure 8.6) or sweat rate (Figure 8.7) responses. This could be considered surprising given the modulation of exercise duration/intensity by thermal and non-thermal cooling and thermal warming. However this could be at least partially explained by the suppression of heart rate (Mundel et al. 2006a) and local sweat rate (Cotter and Taylor 2005) via acute face cooling. Nevertheless, the present study appears to have successfully isolated skin temperature and thermal perception as potential controllers of thermoregulatory behavior.

8.4.2: Conclusions

By thermally and non-thermally cooling or heating the face during self-paced exercise under significant heat stress, the present study independently evaluated (facial) skin temperature and thermal perception as controllers of human thermoregulatory behavior. In utilizing this self-paced exercise model, the present study demonstrates that thermal behavior, defined as the exercise work output, is influenced by changes in thermal sensation and discomfort irrespective of changes in temperature. These data indicate that changes in temperature are not a requirement for the initiation of thermoregulatory behavior in humans. Rather, thermal sensation and, ultimately, thermal discomfort are capable behavioral controllers.

Acknowledgments

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CHAPTER NINE

9.0: Peak Oxygen Uptake: A Determinant of Exercise Intensity in the Heat?

Publication(s) based on this chapter:

Schlader ZJ, Stannard SR, Mundel T. (2011) Is peak oxygen uptake a determinant of moderate duration self-paced exercise performance in the heat? *Appl Physiol Met Nutr* In Press

Abstract

Reductions in peak oxygen uptake ($\dot{V}O_{2\text{peak}}$) and a higher percentage of $\dot{V}O_{2\text{peak}}$ ($\% \dot{V}O_{2\text{peak}}$) at a given intensity have been proposed to reduce exercise intensity in the heat. This study described and compared the cardio-respiratory outcomes of self-paced and peak exercise of eleven male subjects in hot (mean \pm SD; HOT, $40.2 \pm 0.3^\circ\text{C}$) and moderate (MOD; $20.4 \pm 0.7^\circ\text{C}$) conditions. During peak exercise, oxygen uptake ($\dot{V}O_2$) was ~8% higher in HOT, but $\dot{V}O_{2\text{peak}}$ (MOD, 4.64 ± 0.83 L/min; HOT, 4.54 ± 0.77 L/min), peak cardiac output (\dot{Q}_{peak}), and core temperatures (T_C) were similar. During self-paced exercise, $\dot{V}O_2$ was similar through 15 min but was lower in HOT thereafter. Relative to MOD, this represented a higher and lower $\% \dot{V}O_{2\text{peak}}$ during the initial and later stages. Cardiac output was similar in both trials (MOD, 31.6 ± 6.6 L/min; HOT, 30.1 ± 6.0 L/min), representing a similar percentage of \dot{Q}_{peak} throughout. T_C was similar in both conditions until 30 min (MOD, $38.5 \pm 0.3^\circ\text{C}$; HOT, $38.7 \pm 0.3^\circ\text{C}$). These data indicate that when only T_{sk} is elevated, a given exercise intensity elicits a higher $\% \dot{V}O_{2\text{peak}}$, but reductions in exercise intensity are not associated with changes in $\dot{V}O_{2\text{peak}}$.

Keywords

Cardiovascular Strain, Heat Stress, Temperature Regulation, Perceived Exertion, Exercise Intensity

9.1: Introduction

Self-paced exercise intensity is voluntarily reduced in the heat, thereby attenuating exercise performance (Ely et al. 2010; Periard et al. 2011a). Although a characteristic of exhaustion during fixed-intensity exercise (Gonzalez-Alonso et al. 1999; Nybo and Nielsen 2001a), high core temperatures alone do not explain the observed voluntary reductions in exercise intensity. Rather, it appears as though skin temperature (**Chapter Seven**), either by influencing thermal perception (**Chapter Eight**) or via its modulation of cardiovascular responses (Rowell et al. 1969c), plays an important role in the selection of exercise intensity. Accordingly, the relationship between elevated skin temperatures and the cardiovascular consequences has been proposed, explaining attenuations in self-paced exercise performance in the heat (Ely et al. 2010; Periard et al. 2011a). According to this hypothesis, the displacement of blood to the cutaneous vasculature reduces peak cardiac output (\dot{Q}_{peak}) (Rowell et al. 1966), thereby reducing muscle perfusion (Gonzalez-Alonso and Calbet 2003), and therefore peak oxygen uptake ($\dot{V}O_{2\text{peak}}$) (Arngrimsson et al. 2004; Arngrimsson et al. 2003). Therefore, in the heat any given exercise intensity represents a higher percentage of $\dot{V}O_{2\text{peak}}$ ($\% \dot{V}O_{2\text{peak}}$). Thus, sustainable exercise intensity is potentially reduced in the heat (Cheuvront et al. 2010; Periard et al. 2011a), although notably, it remains unclear as to whether a reduction in $\dot{V}O_{2\text{peak}}$ is a pre-requisite for a reduction in sustainable exercise intensity.

The cardiovascular responses to prolonged (~60 min) self-paced exercise in the heat have been recently described by Periard et al. (2011a). As such, increases in cardiovascular strain (i.e. increases in heart rate, and reductions in cardiac output, stroke volume, and mean arterial pressure) were found to be associated with reductions in exercise intensity and $\dot{V}O_{2\text{peak}}$ measured during the final stages of exercise. As proposed previously (Cheuvront et al. 2010), it was concluded that cardiovascular strain attenuated $\dot{V}O_{2\text{peak}}$, and therefore sustainable and peak exercise intensities (Periard et al. 2011a). However, given the elevations in core temperature, these results may not explain the attenuated performance observed during shorter (≤ 30 min) duration self-paced exercise in the heat where exercise intensity is reduced prior to differences in core temperature (Ely et al.

2010). Furthermore, although a reduced $\dot{V}O_{2\text{peak}}$ has been proposed to decrease self-paced exercise performance in the heat (Cheuvront et al. 2010; Periard et al. 2011a), self-selected exercise intensity responses in the heat have yet to be described relative to measured $\dot{V}O_{2\text{peak}}$, \dot{Q}_{peak} and peak heart rate (HR_{peak}).

The purpose of this study was to describe the cardio-respiratory outcomes of relatively short duration (30 min) self-paced exercise in the heat, and to compare these outcomes to peak exercise responses observed in the same environment. Briefly, this was accomplished by measuring, on two separate occasions, the subjects' peak cardio-respiratory responses in hot and moderate conditions. Then, on two more occasions, in the same subjects under the same environmental conditions, these measurements were repeated during 30 min of self-paced exercise. This methodology allowed for comparisons to be made between those responses observed during peak exercise and those occurring during self-paced exercise. Thus, any potential relationships between cardiovascular processes, $\dot{V}O_{2\text{peak}}$, and self-selected exercise intensity could be formally identified. It was hypothesized that $\dot{V}O_{2\text{peak}}$ and \dot{Q}_{peak} would be reduced in the heat relative to that in the moderate condition. During self-paced exercise in the heat it was hypothesized that reductions in exercise intensity would be related to increased cardiovascular strain, and no such relationships will be evident in the moderate condition. Furthermore, it was also hypothesized that oxygen uptake ($\dot{V}O_2$) and cardiac output (\dot{Q}) would be similar between conditions when expressed as a percentage of the measured $\dot{V}O_{2\text{peak}}$ and \dot{Q}_{peak} .

9.2: Methods

9.2.1: Experimental Overview

Eleven male volunteers each completed four experimental bouts of exercise on a cycle ergometer. The first two bouts involved measuring peak cardio-respiratory exercise responses in both a hot (HOT) and a moderate (MOD) environment. The two remaining exercise bouts consisted of 30 min of self-paced exercise in the same thermal environments. All trials took place at the same time of day and there were at least seven

days between each trial. A randomized experimental design was utilized in order to minimize any order effects.

9.2.2: Subjects

Eleven healthy, physically active males agreed to participate in the study. The subjects' characteristics were (mean \pm SD): age, 23 ± 3 y; height, 1.8 ± 0.1 m; weight, 71.6 ± 7.0 kg; percent body fat, $11.3 \pm 4.1\%$. All subjects exercised a minimum of 3 days per week, but were not taking part in any formal exercise training. Each subject was fully informed of the experimental procedures and possible risks before giving informed, written, consent. The protocol was approved by the University Human Ethics Committee and performed according to the Declaration of Helsinki.

9.2.3: Experimental Protocol

All subjects reported to the laboratory on a total of six occasions. These laboratory visits included (in the following order): A preliminary session during which the subjects were informed and familiarized with the experimental procedures. Two sessions during which the subject's peak cardio-respiratory exercise responses were measured in both HOT and MOD; the order of which was randomized. A familiarization session that mimicked the task the subjects were going to undertake during the remaining two laboratory visits, and two trials during which the subjects undertook 30 min of self-paced exercise in either HOT or MOD, which were assigned in a randomized manner.

The ambient conditions in MOD were $20.4 \pm 0.7^\circ\text{C}$, $24 \pm 7\%$ relative humidity, while in HOT they were $40.2 \pm 0.3^\circ\text{C}$ and $14 \pm 6\%$ relative humidity. In both HOT and MOD air speed was 0.5 m/s. The ambient conditions were similar ($P > 0.05$) within experimental trials undertaken in the same thermal environment. Due to differences in thermal sensation, the subjects could not be blinded to the conditions. Likewise, although no attempt was made to deceive the subjects, they were made completely unaware of the research hypotheses. It was assumed that the subjects were not heat acclimatized as the testing was conducted during the southern hemisphere winter/spring months (mean outdoor temperature: $14 \pm 3^\circ\text{C}$).

Pre-trial diet and hydration were controlled and confirmed as mentioned previously (*see Chapter Four*). During the trials subjects wore only cycling shorts and shoes.

On arrival at the laboratory for the peak and self-paced exercise trials, the subjects voided, nude body weight was measured, and a rectal thermistor was self-inserted. A heart rate monitor and skin thermistors were then applied. The subjects then entered the environmental chamber and commenced the appropriate exercise protocol. When the exercise bout was complete the subjects were immediately removed from the environmental chamber, the experimental equipment was promptly removed, and nude body weight was measured.

9.2.4: Peak Exercise Protocols

Approximately 3 weeks before the first experimental trial, subjects reported to the laboratory for measurement of their peak exercise responses in both HOT and MOD. This protocol involved two distinct bouts of exercise on each occasion. Firstly, an incremental exercise test was used to measure $\dot{V}O_{2\text{peak}}$, while subsequently, a steady-state peak exercise bout was completed to estimate \dot{Q}_{peak} and other associated peak cardiovascular responses. These tests were performed on a friction braked cycle ergometer (Monark 818, Sweden). All subsequent exercise bouts were completed on this same ergometer and are briefly described as follows. Via a custom built interface, the cycling cadence, ergometer load, and the corresponding power output, were acquired (PowerLab, ADInstruments, Australia) and recorded (Chart5, ADInstruments, Australia) continually throughout exercise. Changing the ergometer load involved manually turning a dial located on the ergometer, which directly changed the resistance on the ergometer wheel.

During the incremental exercise tests the subjects were required to maintain a self-selected cycling cadence (mean: 91 ± 6 rpm), while the researcher adjusted the ergometer load accordingly. This test commenced at a power output of 100 W and increased by 50 W every 2 min in a stepwise manner until volitional exhaustion, defined as the inability

to maintain a cadence within 10 rpm of the pre-established cadence. The final power output that was achieved and maintained for 1 min was considered peak power output. During the incremental exercise tests the subjects were able to monitor their cycling cadence, but were unaware of exercise time, power output, ergometer load, or heart rate. Expired gases were collected and analyzed continually (see below). $\dot{V}O_{2\text{peak}}$ was defined as the average $\dot{V}O_2$ during the last full minute completed, i.e. $\dot{V}O_2$ at peak power output. Given that $\dot{V}O_{2\text{peak}}$ was expected to be lower in HOT than in MOD, the result obtained in MOD was considered the control $\dot{V}O_{2\text{peak}}$ if it was within 5% of the ACSM prediction equation (ACSM 2000) with a final rating of perceived exertion (RPE) ≥ 19 (Periard et al. 2011a). The average heart rate at peak power output in a given condition was defined as HR_{peak}. Immediately prior to commencement, during and upon completion of exercise, $\dot{V}O_2$, heart rate, mean skin temperature (\bar{T}_{sk}) and core body temperature (T_C) were measured and recorded every two min, while thermal discomfort, thermal sensation and perceived exertion were measured at exhaustion. Whole body sweat rate was measured pre- to post-exercise.

The steady-state peak exercise bout commenced ~20 min following completion of the incremental exercise test, during which time the subjects rested, seated, in the environmental chamber. This second bout of exercise consisted of ~4 min of steady state peak exercise at a power output aimed to elicit a $\dot{V}O_2$ within 5% of the measured $\dot{V}O_{2\text{peak}}$ (Schlader et al. 2010) or within 5 bpm of HR_{peak} (Arngrimsson et al. 2003). This exercise bout commenced at peak power output. However, from pilot testing, it was determined that these subjects were unlikely to maintain this power output for the entire 4+ min period. Therefore, within the first 30 s of exercise the researcher adjusted the power output until the subject deemed the intensity adequate to successfully complete the 4 min period, yet intense enough that they would not be able to continue beyond 5 min. Following 3 min of exercise at this intensity, steady-state respiratory gases, blood pressure and heart rate were measured, and following exactly 4 min of exercise the CO₂ rebreathing procedures used to estimate \dot{Q}_{peak} were performed. The subjects were familiarized with all of these procedures during their preliminary visit to the laboratory.

9.2.5: Familiarization Session

Approximately one week before the first experimental trial, all subjects completed a familiarization session in which they completed the same self-paced cycling exercise bout that they would subsequently complete. This exercise bout took place in the laboratory in moderate ambient conditions ($20.1 \pm 0.9^{\circ}\text{C}$).

9.2.6: Self-Paced Exercise Protocol

Approximately one week following the familiarization session subjects arrived at the laboratory to undertake self-paced cycling exercise in either HOT or MOD. These experimental trials consisted of a standardized 5 min warm-up (at 100 W) which transitioned into the self-paced cycling exercise protocol. This self-paced exercise bout required the subjects to complete the greatest amount of work as possible in 30 min. Subjects were free to change their cadence and/or the ergometer load. Subjects were verbally encouraged by the same researcher at random intervals and were aware of every 5 min time interval, but had no indication of work completed, cycling cadence, ergometer load, power output or heart rate.

Immediately prior to commencement, during, and upon completion of exercise, power output, heart rate, \bar{T}_{sk} , T_{C} , thermal discomfort, thermal sensation, RPE, and expired gases were measured and recorded every 5 min. Blood pressure was measured every 10 min which was followed by completion of the CO_2 rebreathing procedures. Whole body sweat rate was determined pre- to post-exercise, while total work completed was recorded upon exercise completion.

9.2.7: Measurements

Anthropometric characteristics, heart rate, \bar{T}_{sk} , RPE, thermal discomfort and thermal sensation were measured as described previously (*see Chapter Four*).

Rectal temperature served as an index of core body temperature, and was measured with a rectal thermistor (Mon-a-therm, Tyco Healthcare Group, USA) inserted 10 cm beyond the anal sphincter.

During all trials expired gases were analyzed using the same online system (Turbofit, Vacumed, USA). During the peak exercise protocols expired gases were collected and analyzed continually, and recorded as mentioned previously (see above). During the self-paced exercise trials expired gases were collected and analyzed for two consecutive min at every recording interval, and mean $\dot{V}O_2$, CO_2 elimination, respiratory exchange ratio (RER), and expiratory minute ventilation during the final min of this collection period were recorded.

Cardiac output (\dot{Q}) was estimated via the indirect Fick equation: $\dot{V}CO_2 = \dot{Q}/A - V CO_2$ where: $\dot{V}CO_2$ is the rate of carbon dioxide elimination and A-V CO_2 is the arteriovenous CO_2 content difference. $\dot{V}CO_2$ was measured from the expired gases (see below) while A-V CO_2 was calculated from the estimated venous and arterial PCO_2 (McHardy 1967). Arterial PCO_2 was estimated from the end-tidal CO_2 data ($PETCO_2$) measured prior to the rebreathing procedure and corrected as demonstrated by Jones et al. (1979), while venous PCO_2 was estimated via the CO_2 rebreathing method described by DeFares (1958) and corrected according to Paterson and Cunningham (1976). The CO_2 rebreathing procedures involved the subjects rebreathing from an anaesthesia bag filled with a gas mixture containing 4% CO_2 , 35% O_2 , and the balance nitrogen. The volume of this rebreathing bag was approximately that of tidal volume as measured during the preliminary session. The high O_2 concentration utilized presently was employed in order to minimize hypoxemia, assuring full oxygenation of the blood during rebreathing (Ohlsson and Wranne 1986). The rebreathing procedure commenced when the $PETCO_2$ values were stable, upon which the rebreathing valve was opened and the rebreathing commenced. CO_2 rebreathing lasted approximately 15 s, during which an exponential capnograph tracing was produced, allowing for estimation of venous PCO_2 (DeFares 1958). All $PETCO_2$ data were measured (O_2/CO_2 Gas Analyzer, ADInstruments, Australia), acquired (PowerLab, ADInstruments, Australia), and displayed (Chart5,

ADInstruments, Australia) continuously throughout the entire procedure. Stroke volume was calculated from the Fick equation. Blood pressure was measured in duplicate manually using a stethoscope and a sphygmomanometer over the right brachial artery. All blood pressure measurements were made by the same experienced operator. Mean arterial pressure (MAP, in mmHg) was estimated by auscultation of the systolic (SBP) and diastolic blood pressure (DBP) according to the following equation: $MAP = DBP + 1/3 * (SBP - DBP)$. Oxygen pulse was calculated as $\dot{V}O_2$ (in ml/min) divided by heart rate. Total peripheral resistance (TPR, in mmHg/L/min) was calculated as MAP divided by \dot{Q} . The arteriovenous oxygen difference (A-V O_2 , in ml/100 ml) was estimated according to the following equation: $A - V O_2 = \dot{V}O_2 / \dot{Q} * 100$.

After correcting for respiratory and metabolic water losses (Mitchell et al. 1972), changes in nude body weight were used to estimate whole body sweat rate according to the following equation: Whole body sweat rate (in g/min) = (Initial body weight - final body weight) + ($\dot{V}O_2 \cdot (RER \cdot 1.96 - 1.43)$) + ($0.019 \cdot \dot{V}O_2 \cdot (44 - P_A)$).

9.2.8: Statistical Analysis

Mean differences between trials were compared via paired *t*-tests. To identify any changes in dependent variables during exercise in both the peak and self-paced exercise protocols, a two-way (trial x time) repeated measures analysis of variance (ANOVA) was conducted. These data were assessed for approximation to a normal distribution and sphericity, and no corrections were necessary. When the two-way ANOVA revealed a significant *F* test, *post hoc* pair-wise comparisons were made incorporating a Bonferroni adjustment. Relationships between the mean cardio-respiratory measures and mean self-selected power output were evaluated using Pearson product moment correlation analysis. Using conventional α (0.05) and β (0.20) parameters and a moderate effect size (0.8), based on the data collected in the previous studies included in this thesis, eleven subjects was deemed appropriate in order to detect meaningful differences (Tran 1997) in the primary dependent variables (e.g. power output, $\dot{V}O_{2peak}$, etc.). All data were analyzed using SPSS statistical software (V. 15, Chicago, IL, USA) with *a priori*

statistical significance set at $P < 0.05$. All data are reported as mean \pm SD unless otherwise noted.

9.3: Results

9.3.1: Incremental Exercise Test

$\dot{V}O_2$ was $8 \pm 2\%$ higher ($P < 0.05$) at a given submaximal exercise intensity in HOT compared to MOD (Figure 9.1) and, with increasing exercise intensity, RER increased ($P < 0.01$) similarly ($P > 0.05$) between conditions (Final RER – HOT: 1.15 ± 0.06 ; MOD: 1.16 ± 0.08). Exercise duration was longer ($P < 0.05$) in MOD (10.2 ± 2.2 min) than in HOT (9.8 ± 2.1 min), but peak power output was similar ($P > 0.05$) in both conditions (HOT: 295 ± 52 W; MOD: 305 ± 57 W). $\dot{V}O_{2peak}$ was similar ($P > 0.05$) between conditions (HOT: 4.54 ± 0.77 L/min; MOD: 4.64 ± 0.83 L/min; Figure 9.1), while heart rate (HOT: 182 ± 7 bpm; MOD: 177 ± 8 bpm) and O_2 pulse (HOT: 25.0 ± 4.5 ml O_2 /beat; MOD: 26.3 ± 5.3 ml O_2 /beat) were higher ($P < 0.05$) and lower ($P < 0.05$) in HOT compared to MOD.

\bar{T}_{sk} was higher ($P < 0.001$) in HOT ($36.5 \pm 0.5^\circ\text{C}$) than in MOD ($31.6 \pm 1.6^\circ\text{C}$), but initial (HOT: $37.0 \pm 0.4^\circ\text{C}$; MOD: $37.1 \pm 0.4^\circ\text{C}$) and final (HOT: $37.3 \pm 0.3^\circ\text{C}$; MOD: $37.4 \pm 0.4^\circ\text{C}$) T_c were similar ($P > 0.05$) in the two conditions. The change in T_c (HOT: $+0.3 \pm 0.2^\circ\text{C}$, MOD: $+0.3 \pm 0.2^\circ\text{C}$) and the rate of rise in T_c (HOT: $0.0284 \pm 0.0135^\circ\text{C}/\text{min}$, MOD: $0.0315 \pm 0.0148^\circ\text{C}/\text{min}$) were similar ($P > 0.05$) in both conditions. The core-to-skin temperature gradient at peak power output was lower ($P < 0.001$) in HOT ($0.8 \pm 0.4^\circ\text{C}$) than in MOD ($6.1 \pm 1.2^\circ\text{C}$).

Upon exhaustion, RPE was similar ($P > 0.05$) between HOT (19.0 ± 0.3) and MOD (19.0 ± 0.2), while subjects reported being more ($P < 0.05$) thermally uncomfortable (HOT: 3.4 ± 0.5 , MOD: 2.7 ± 0.7) and warmer (HOT: 6.4 ± 0.5 , MOD: 5.7 ± 0.6) in HOT. Whole body sweat rate was higher ($P < 0.001$) in HOT (23.2 ± 5.7 g/min) compared to MOD (15.9 ± 4.7 g/min).

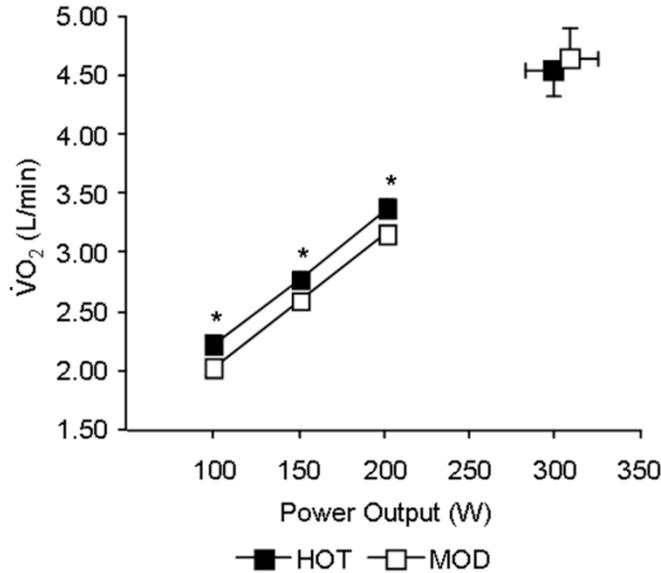


Figure 9.1: Oxygen consumption ($\dot{V}O_2$) during incremental exercise to exhaustion in hot (HOT) and moderate (MOD) thermal environments (mean \pm SE). * denotes significantly different than MOD ($P < 0.05$).

9.3.2: Steady-State Peak Exercise

$\dot{V}O_2$ and heart rate both increased ($P < 0.001$) over time in HOT and MOD through 3 min of exercise. However, there were no differences ($P > 0.05$) between 3 min and 4 min for either $\dot{V}O_2$ (HOT: 3 min, 4.37 ± 0.81 L/min, 4 min, 4.38 ± 0.79 L/min; MOD: 3 min 4.24 ± 0.78 L/min, 4 min, 4.28 ± 0.81 L/min) or heart rate (HOT: 3 min, 182 ± 8 bpm, 4 min, 183 ± 7 bpm; MOD: 3 min 176 ± 9 bpm, 4 min, 176 ± 10 bpm) in both conditions, indicating a steady-state was attained. In both HOT and MOD ($P > 0.05$), only $93 \pm 7\%$ of $\dot{V}O_{2peak}$ was elicited (Table 9.1). Notably however, heart rates were within $99.9 \pm 1.2\%$ of HR_{peak} (Table 9.1). Aside from heart rate ($P < 0.001$), \bar{T}_{sk} ($P < 0.001$), and the core-to-skin temperature gradient ($P < 0.001$), all other cardio-respiratory variables were similar ($P > 0.05$) between conditions (Table 9.1).

Table 9.1: Cardiovascular responses during steady-state peak exercise in moderate and hot thermal environments (mean \pm SD).

	Moderate	Hot
$\dot{V}O_2$ (L/min)	4.28 \pm 0.81	4.38 \pm 0.79
% $\dot{V}O_2$ peak (%)	92.6 \pm 5.5	93.8 \pm 8.5
RER	1.00 \pm 0.06	1.01 \pm 0.04
Heart Rate (bpm)	176 \pm 10	183 \pm 7 *
%HRpeak (%)	100.0 \pm 0.0	99.8 \pm 2.4
O ₂ Pulse (ml O ₂ /beat)	24.5 \pm 5.4	24.0 \pm 4.8
Power Output (W)	265 \pm 56	248 \pm 64
MAP (mmHg)	124 \pm 8	124 \pm 8
\dot{Q} peak (L/min)	33.9 \pm 3.4	33.8 \pm 4.5
Stroke Volume (ml)	193 \pm 24	185 \pm 28
TPR (mmHg/L/min)	3.7 \pm 0.6	3.7 \pm 0.6
A-V O ₂ (ml/100 ml)	12.6 \pm 1.5	12.9 \pm 1.4
T _C (°C)	37.8 \pm 0.4	37.9 \pm 0.4
\bar{T}_{Sk} (°C)	31.2 \pm 1.5	36.6 \pm 0.6 *
Core-to-Skin Gradient (°C)	5.8 \pm 1.4	0.8 \pm 0.4 *

$\dot{V}O_2$ peak, peak oxygen uptake; % $\dot{V}O_2$ peak, percent of $\dot{V}O_2$ peak; RER, respiratory exchange ratio; %HRpeak, percent of peak heart rate; MAP, mean arterial pressure; \dot{Q} peak, peak cardiac output; TPR, total peripheral resistance; A-V O₂, arteriovenous oxygen difference, T_C, core body temperature; \bar{T}_{Sk} , mean skin temperature. * indicates significantly different than Moderate (P<0.01).

9.3.3: Self-Paced Exercise

9.3.3.1: Total Work and Power Output

Total work completed in HOT was 21 \pm 5% lower (P<0.001) than that in MOD (HOT: 271.5 \pm 58.4 kJ, MOD: 346.6 \pm 79.7 kJ). This decrement in performance was due to a 22 \pm 6% lower (P<0.01) mean power output (HOT: 154 \pm 33 W, MOD: 201 \pm 56 W; Figure 9.2).

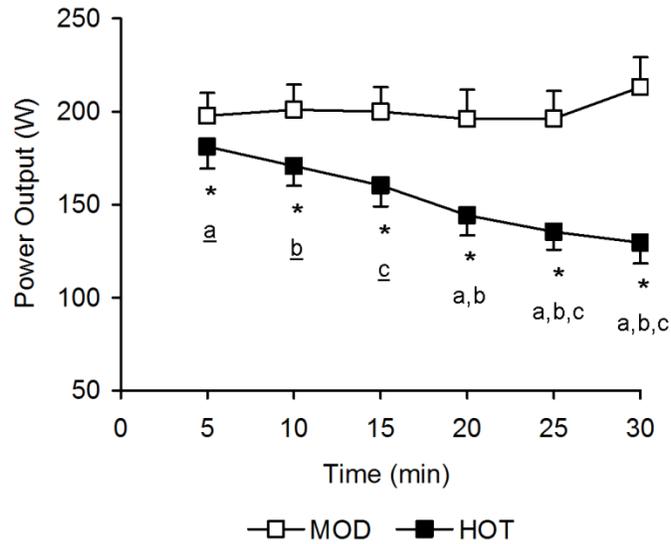


Figure 9.2: Power output responses during self-paced exercise in hot (HOT) and moderate (MOD) thermal environments (mean \pm SE). * indicates significantly different than MOD ($P < 0.05$); Letters indicate significant differences ($P < 0.05$) between underlined and the subsequent time points within the same condition.

9.3.3.2: Thermoregulatory Measures

Pre-exercise (i.e. pre- warm-up) T_C was similar ($P > 0.05$) between trials (MOD: $37.2 \pm 0.4^\circ\text{C}$; HOT: $37.2 \pm 0.4^\circ\text{C}$), and rose ($P < 0.01$) similarly ($P > 0.05$) in both HOT and MOD through 25 min of exercise. However, final T_C (at 30 min) was higher ($P < 0.05$) in HOT ($38.7 \pm 0.3^\circ\text{C}$) than in MOD ($38.5 \pm 0.3^\circ\text{C}$). \bar{T}_{sk} was higher ($P < 0.001$) throughout in HOT, but increased ($P < 0.01$) over time in both trials. The core-to-skin temperature gradient was lower ($P < 0.001$) throughout exercise in HOT ($0.9 \pm 0.3^\circ\text{C}$) compared to MOD ($5.7 \pm 0.9^\circ\text{C}$).

9.3.3.3: Cardio-Respiratory Measures

Through 15 min of exercise $\dot{V}O_2$ was similar ($P > 0.05$; Figure 9.3A), which resulted in a higher ($P < 0.05$) % $\dot{V}O_{2peak}$ in HOT at 10 min (Figure 9.3B). After 15 min, $\dot{V}O_2$ was lower ($P < 0.05$) in HOT (Figure 9.3A).

Cardiac output did not change ($P>0.05$) over time and was similar ($P>0.05$) between trials (Figure 9.4E). Mean arterial pressure was similar ($P>0.05$) at 10 min, but was lower ($P<0.05$) in HOT at 20 and 30 min (Figure 9.4A). Stroke volume was similar ($P>0.05$) through 20 min, but was lower ($P<0.05$) in HOT at 30 min (Figure 9.4D). Heart rate increased ($P<0.001$) over time in both trials, but between 10 min and 20 min was higher ($P<0.05$) in HOT (Figure 9.4B). Cardiac output and heart rate during self-paced exercise represented similar ($P>0.05$) percentages of \dot{Q}_{peak} (Figure 9.4F) and HR_{peak} (Figure 9.4C) in both conditions.

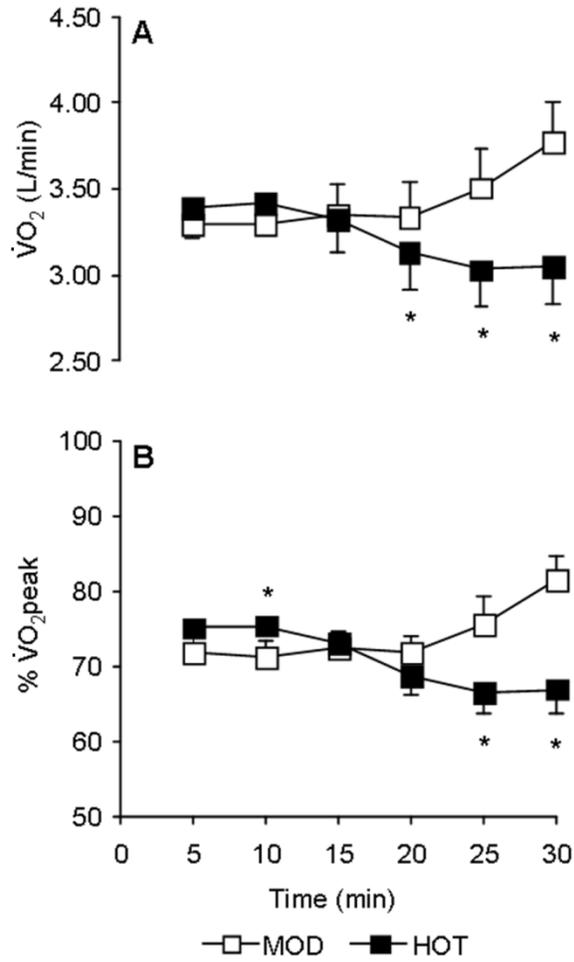


Figure 9.3: Oxygen consumption ($\dot{V}O_2$) during self-paced exercise in hot (HOT) and moderate (MOD) thermal environments, expressed as absolute values (A) and as a percentage of measured peak $\dot{V}O_2$ (% $\dot{V}O_{2peak}$; B; mean \pm SE). * denotes significantly different than MOD ($P < 0.05$).

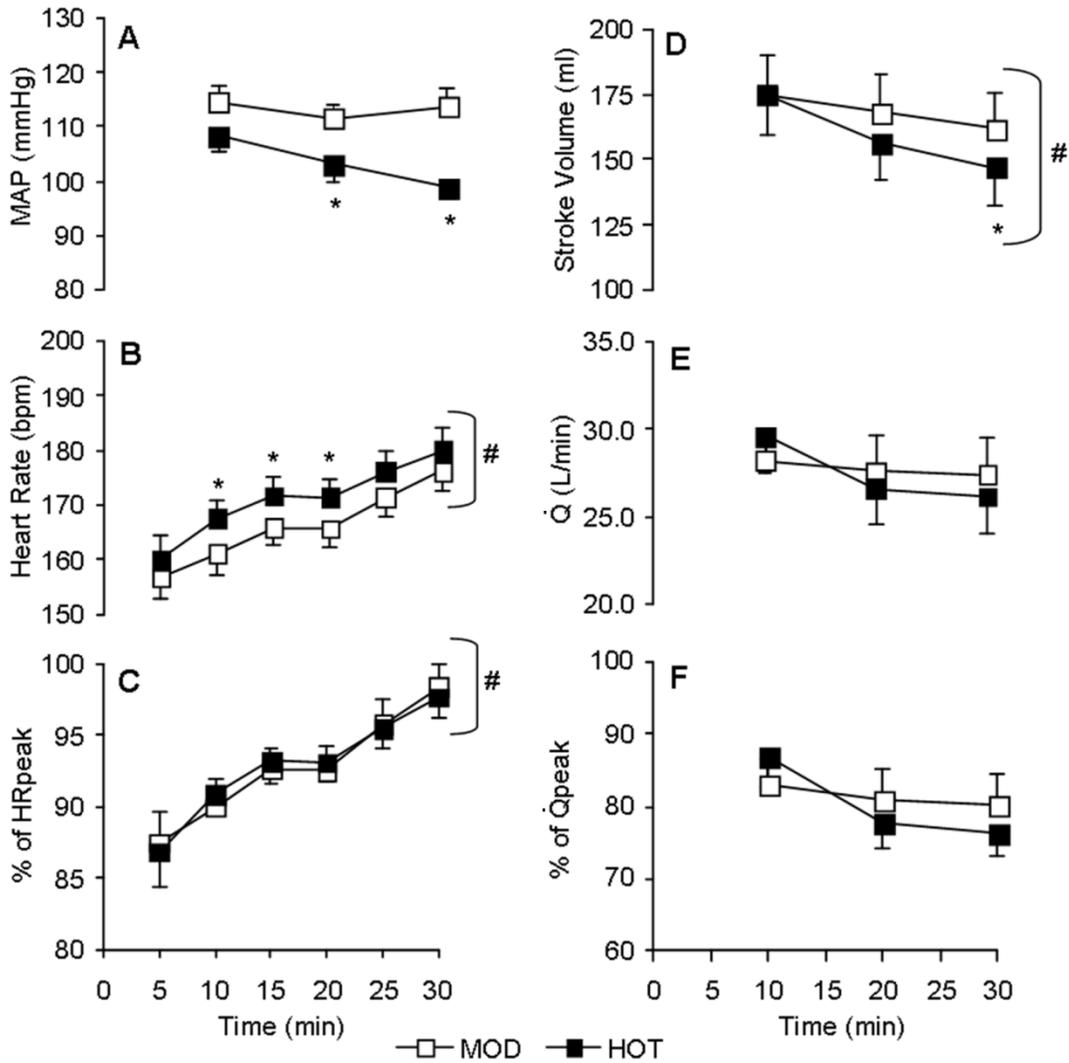


Figure 9.4: Mean arterial pressure (MAP; A), , heart rate (B), heart rate presented as a percentage of measured peak heart rate (% of HRpeak; C), stroke volume (D), cardiac output (\dot{Q} ; E), and \dot{Q} presented as a percentage of measured peak cardiac output (% of \dot{Q} peak; F) during self-paced exercise in hot (HOT) and moderate (MOD) thermal environments (mean \pm SE). * denotes significantly different than MOD ($P < 0.05$); # denotes significant main effect of time ($P < 0.01$).

9.3.3.4: Sweat Rate and Perceptions

RPE increased ($P < 0.01$) similarly ($P > 0.05$) over time in both trials (Figure 9.5). Sensations of warmth and thermal discomfort increased ($P < 0.001$) in both MOD and

HOT, but both warmth and thermal discomfort were higher ($P < 0.001$) in HOT throughout exercise. Whole body sweat rate was higher ($P < 0.001$) in HOT (23.0 ± 6.7 g/min) than in MOD (16.1 ± 4.3 g/min).

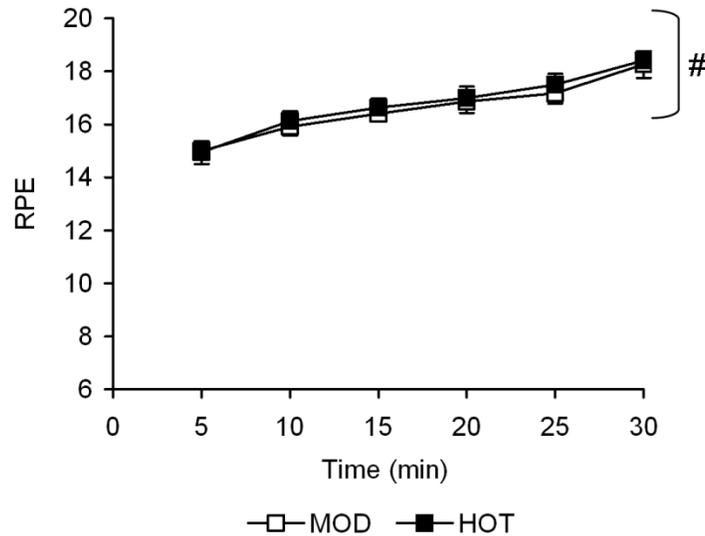


Figure 9.5: Ratings of perceived exertion (RPE) during self-paced exercise in hot (HOT) and moderate (MOD) thermal environments (mean \pm SE). # denotes significant main effect of time ($P < 0.01$).

9.3.3.5: Correlation Analysis

In MOD power output was not found to be related ($P > 0.05$) to heart rate ($r = 0.565$), MAP ($r = 0.727$), \dot{Q} ($r = -0.458$), stroke volume ($r = -0.654$), $\dot{V}O_2$ ($r = 0.778$), $\% \dot{V}O_{2\text{peak}}$ ($r = 0.798$), or $\% \dot{Q}_{\text{peak}}$ ($r = -0.537$). By contrast heart rate ($r = -0.940$), MAP ($r = 0.995$), \dot{Q} ($r = 0.974$) stroke volume ($r = 0.999$), $\dot{V}O_2$ ($r = 0.964$), $\% \dot{V}O_{2\text{peak}}$ ($r = 0.973$), and $\% \dot{Q}_{\text{peak}}$ ($r = 0.982$) were correlated ($P < 0.05$) with power output responses in HOT.

9.4: Discussion

The primary objective of this investigation was to describe the cardio-respiratory responses to self-paced exercise in the heat, and to evaluate these relative to those observed during peak exercise in the same environment. Thus, this study attempted to identify potential relationships between cardiovascular processes, $\dot{V}O_{2\text{peak}}$, and self-selected exercise intensity. Consequently, these data support the hypothesis that any given submaximal exercise intensity elicits a higher % $\dot{V}O_{2\text{peak}}$ in the heat. Furthermore, the data presented also confirm that voluntary reductions in exercise intensity are associated with increases in heart rate and reductions in stroke volume, mean arterial pressure and $\dot{V}O_2$. However, in the current study alterations in \dot{Q}_{peak} and $\dot{V}O_{2\text{peak}}$ do not appear to account for the attenuation in exercise performance. Rather, this performance decrement may be related to an increased $\dot{V}O_2$ at a given submaximal exercise intensity.

Increases in cardiovascular strain have been identified as factors associated with reductions in exercise intensity in the heat (Periard et al. 2011a), and indeed, the data presented in the current study do suggest a role for many of these responses (Figure 9.3 and Figure 9.4). However, given the apparent importance of $\dot{V}O_{2\text{peak}}$ and % $\dot{V}O_{2\text{peak}}$ in prolonged exercise performance (Bassett and Howley 2000), it is most likely that the relationship between cardiovascular strain and reductions in exercise intensity are ultimately manifested in alterations in $\dot{V}O_{2\text{peak}}$ (Cheuvront et al. 2010). Thus, as hypothesized, alterations in $\dot{V}O_{2\text{peak}}$ have been suggested to explain the observed voluntary reductions in exercise intensity (Ely et al. 2010; Periard et al. 2011a). This hypothesis is predicated from observations that, when both core and skin temperatures are substantially elevated, $\dot{V}O_{2\text{peak}}$ is reduced during incremental exercise (Arngrimsson et al. 2004; Arngrimsson et al. 2003) and following self-paced exercise (Periard et al. 2011a) in the heat. Under these circumstances, it appears that reductions in \dot{Q}_{peak} reduce blood pressure (Rowell et al. 1966) and consequently active muscle blood flow (Gonzalez-Alonso and Calbet 2003). Therefore, a given exercise intensity in the heat would elicit a higher % $\dot{V}O_{2\text{peak}}$ (Cheuvront et al. 2010). However, \dot{Q}_{peak} is not always

affected by heat stress (Williams et al. 1962), perhaps explaining the observation that $\dot{V}O_{2peak}$ is minimally affected when only skin temperatures are elevated (Arngrimsson et al. 2004; Rowell et al. 1969b; Williams et al. 1962). In the current study, \dot{Q}_{peak} (Table 9.1) and $\dot{V}O_{2peak}$ (Figure 9.1) were not significantly affected by elevations in skin temperature. Consequently, the $\dot{V}O_2$ (Figure 9.3A) and cardiac output (Figure 9.4E) responses to self-paced exercise expressed as $\% \dot{V}O_{2peak}$ (Figure 9.3B) and $\% \dot{Q}_{peak}$ (Figure 9.4F) could not be adequately explained by changes in peak cardio-respiratory responses. Therefore, in the current paradigm thermal alterations to these peak exercise responses are unlikely to explain the observed exercise intensity responses, perhaps demonstrating that reductions in sustainable exercise intensity are not always causally associated with reductions in $\dot{V}O_{2peak}$.

During moderate intensity exercise in the heat, progressive reductions in stroke volume are effectively countered by increases in heart rate and reductions in visceral blood flow in order to maintain (Rowell et al. 1966; Williams et al. 1962) or enhance (Nielsen et al. 1984) cardiac output so that blood pressure is maintained. In the current study, cardiac output was similar in both the hot and moderate conditions (Figure 9.4E) despite reductions in exercise intensity (Figure 9.2) and $\dot{V}O_2$ (Figure 9.3A). The metabolic consequences are likely described by the observation that $\dot{V}O_2$ at a given submaximal exercise intensity was found to be higher in the heat (Figure 9.1), i.e. gross efficiency was reduced (Hettinga et al. 2007). This finding corroborates with previous research (e.g. Hettinga et al. 2007), but conflicts with the findings of other studies (Rowell et al. 1969b; Williams et al. 1962). Nevertheless, reduced gross efficiency may partially explain the selection of a lower exercise intensity in the heat (Hettinga et al. 2007). In the current paradigm, during the initial stages of exercise it appears as though an exercise intensity was selected that would elicit a similar absolute $\dot{V}O_2$ (Figure 9.3A). As a consequence of reduced gross efficiency at submaximal exercise intensities (Figure 9.1), this intensity was lower in the heat (Figure 9.2). The observed reduction in gross efficiency is unlikely to be explained by critically high muscle temperatures (i.e. $>40^{\circ}C$) (Nybo 2008), but could be described by increases in the resting metabolic rate associated with increases in

body temperature (Saxton 1981); a process known to reduce gross efficiency (Hettinga et al. 2007).

In the current paradigm, given the large discrepancies in the core-to-skin temperature gradient, exercise intensity, and therefore the blood flow required by the working musculature, appears to have been voluntarily reduced in order to ensure an adequate portion of the cardiac output was directed towards the skin for thermoregulatory purposes. Together with an enhanced sweat rate, these responses appear to have maintained core body temperature similarly throughout most of the exercise task. These observations can adequately explain previous findings that the core temperature response to moderate duration (≤ 30 min) self-paced exercise is similar in both hot and more moderate conditions (Ely et al. 2010). Likewise, these responses also ensured core temperatures remain below those levels commonly deemed as critical (Nybo 2008), but at the expense of exercise performance.

9.4.1: Considerations and Limitations

Current evidence suggests that self-selected exercise intensity is mediated primarily by the perception of effort response (Joseph et al. 2008) (**Chapter Six, Chapter Seven, Chapter Eight**). As such, irrespective of the trial length or ambient conditions, during self-paced exercise the perception of effort increases relative to the proportion of the exercise bout completed (Joseph et al. 2008) (**Chapter Six, Chapter Seven, Chapter Eight**), as was observed currently (Figure 9.5). These findings suggest that subjects are comparing how they feel, to how they expected themselves to feel at that moment and adjusting their exercise intensity accordingly (Joseph et al. 2008). Under heat stress, elevations in skin temperature, independent of differences in core temperature, have been shown to increase the perception of effort at a given exercise intensity (Pivarnik et al. 1988). Thus, elevated skin temperatures are important in the voluntary selection of exercise intensity (**Chapter Seven**).

As the present study has investigated, elevations in skin temperature have cardio-respiratory implications which may ultimately drive the perception of effort response, and

therefore the selection of exercise intensity. For instance, heart rate is a potential mediator of the perception of effort (Borg 1982), and heart rate is elevated with increases in skin temperature (Rowell et al. 1969c). Thus, elevated skin temperatures could mediate the reductions in exercise intensity through its effects on heart rate and thus, perceived exertion. However, this appears unlikely as there is evidence indicating the relationship between perceived exertion and heart rate is dissociated in the heat (Pandolf 1977). Another likely perceived exertion input worthy of consideration is absolute $\dot{V}O_2$ (Toner et al. 1986). However, in the current study, similar to that observed previously (Lollgen et al. 1977), these two variables appear disconnected during the later stages of self-paced exercise in the heat (Figure 9.3A and Figure 9.5). A final input perhaps modulating the perception of effort during exercise in the heat is $\% \dot{V}O_{2peak}$. This is especially notable as $\% \dot{V}O_{2peak}$ is not only a key factor in the performance of muscular exercise (Bassett and Howley 2000), but is also an important signal in the perception of effort (Pandolf et al. 1984). Thus, it is perhaps not unexpected that reductions in $\dot{V}O_{2peak}$, and therefore increases in $\% \dot{V}O_{2peak}$ at any given exercise intensity, have been suggested as the ultimate reason for exercise performance being reduced in the heat (Cheuvront et al. 2010). Notably however, as observed in the current study (Figure 9.3B and Figure 9.5), the relationship between the perception of effort and $\% \dot{V}O_{2peak}$ is distorted under thermal stress (Pivarnik et al. 1988; Toner et al. 1986). This suggests that $\% \dot{V}O_{2peak}$ may not be a suitable input for the perception of effort, and therefore the selection of exercise intensity, in the heat.

Assuming the perception of effort is the definitive modulator of self-selected exercise intensity (Joseph et al. 2008) (**Chapter Six, Chapter Seven, Chapter Eight**), it appears most likely that the thermal responses directly related to elevated skin temperatures (Noble and Robertson 1996) offer the most plausible explanation for voluntary reductions in exercise intensity under heat stress. Although further research is needed, it is notable that thermal perception has been recently found to independently modulate the perception of effort, and thus exercise intensity, in the heat (**Chapter Eight**).

Some of the findings and conclusions made herein may be limited by the protocols and methods utilized. For instance, given the relatively large stepwise increments in exercise intensity (i.e. 50 W) it is possible that relatively small changes in $\dot{V}O_{2\text{peak}}$ or peak power output may not have been appropriately identified. Notably however, the incremental exercise protocol used ensured a relatively short exercise duration, thereby limiting changes in core body temperature that could have potentially restricted the ability to transfer the findings to the subsequent self-paced trials. Additionally, given that it elicited only ~93% of $\dot{V}O_{2\text{peak}}$ (Table 9.1), the steady-state peak exercise protocol may have underestimated \dot{Q}_{peak} . However, this protocol did elicit nearly 100% of HR_{peak} in both conditions (Table 9.1), and thus we are confident that a peak exercise response was indeed elicited (Arngrimsson et al. 2003).

It is further recognized that the core temperature measurement location utilized is a relatively slow changing index, and thus may have underestimated dynamic changes in core body temperature. Likewise, estimates of mean skin temperature are improved by increasing skin temperature measurement locations; thus, the four-site estimate of mean skin temperature used in this study may be inaccurate. However, given that this subject cohort had a remarkably low percent body fat, that skin temperatures would not be considered 'cold' (Livingstone et al. 1987), and that thermal sensation coincided similarly with changes in measured skin temperature, an inaccurate estimate appears unlikely. Furthermore, due to the self-paced nature of the exercise, the derivation of cardiac output from CO_2 rebreathing may have resulted in an inaccurate estimation of cardiac output. However, these methods appear adequate in non-steady-state exercise situations (McKelvie et al. 1987) and are comparable to previous findings during self-paced exercise in subjects with similar $\dot{V}O_{2\text{peak}}$ values (Periard et al. 2011a).

Finally, it can be argued that the measurements made during the peak exercise bouts are not transferrable to those made during the self-paced exercise bouts. For instance, $\dot{V}O_{2\text{peak}}$ measured in the heat was accompanied by lower absolute core temperatures and it is likely that if $\dot{V}O_{2\text{peak}}$ was measured when core and skin temperatures were similar

to those occurring during the self-paced exercise bout, reductions in $\dot{V}O_{2\text{peak}}$ would likely account for a larger proportion of the reductions in exercise intensity. However, given that the displacement of blood towards the cutaneous vasculature is driven predominantly by the core-to-skin temperature gradient (Kerslake 1972) and that the core-to-skin temperature gradients were remarkably similar in the peak and the self-paced exercise bouts, it can be reasonably assumed that the thermally mediated cardiovascular processes were similar between exercise bouts undertaken in the same thermal environment. Therefore, the results obtained during the peak exercise trials are likely transferable to the self-paced exercise trials.

9.4.2: Conclusions

The aim of this study was to describe, relative to peak exercise responses, the cardio-respiratory outcomes of relatively short duration self-paced exercise in the heat. Therefore, during instances when only skin temperatures were substantially elevated, this study attempted to identify potential cardio-respiratory factors related to reductions in exercise performance in the heat. Under this paradigm, the data presented support previous work indicating that self-selected exercise intensity in the heat is associated with increases in heart rate and reductions in stroke volume, mean arterial pressure, and $\dot{V}O_2$, and support the proposal that a given submaximal exercise intensity elicits a higher % $\dot{V}O_{2\text{peak}}$ in the heat. However, these responses do not appear to be associated with changes in \dot{Q}_{peak} or $\dot{V}O_{2\text{peak}}$. Rather, increases in $\dot{V}O_2$ at a given submaximal exercise intensity appear to play a larger role in the voluntary decision to reduce exercise intensity in the heat. As this study was purely descriptive in nature, further, more mechanistic, studies are warranted.

Acknowledgments

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CHAPTER TEN

10.0: General Discussion

The purpose of the cohort of studies presented in this thesis was to further elucidate the control of human thermoregulatory behavior by using a self-paced exercise and exogenous heat stress model. General Aims I and II were established in order to accomplish this objective. General Aim I involved testing the hypothesis that self-selected exercise intensity responses in the heat are thermoregulatory behaviors. It was hoped that the data collected toward this aim would help establish self-paced exercise in the heat as an experimental model for human thermal behavior. In accordance, the studies presented in **Chapter Five** and **Chapter Six** observed voluntarily selected exercise intensity responses with direct reference to this hypothesis. As General Aim I found associative evidence for thermoregulatory behavior during self-paced exercise in the heat, General Aim II intended to identify the manner in which these specific behavioral responses were controlled. In accordance, \bar{T}_{sk} (**Chapter Seven**), thermal perception (**Chapter Eight**), and $\dot{V}O_{2peak}$ (**Chapter Nine**) were formally tested as potential modulators of exercise intensity.

10.1: General Aim I

With direct regards for General Aim I, **Chapter Five** directly evaluated exercise modality as a modulator of body temperature regulation in the heat. In accordance, thermoregulatory, cardiovascular and heat exchange responses were compared during work-matched fixed-intensity and self-paced exercise in uncompensable heat stress. It was found that voluntary reductions in exercise intensity during self-paced exercise improved thermal compensability, thereby reducing thermoregulatory and physiological strain. Thus, exercise modality modulated body temperature regulation, providing evidence of a potential role for thermal behavior during exercise in the heat.

Subsequently, by evaluating the behavioral and thermal outcomes against specific, pre-defined, criteria, **Chapter Six** aimed to identify reductions in exercise intensity occurring

during self-paced exercise in the heat as thermoregulatory behaviors. It was therefore demonstrated that reductions in exercise intensity occurring in the heat were consistent responses that presumably aided heat exchange over time, allowing for the attainment of heat balance. Furthermore, changes in exercise intensity were found to involve a conscious decision, and were associated with increases in thermal discomfort and total body heat storage. Finally, and perhaps most importantly, there was no evidence for thermal behavior when self-paced exercise is undertaken in cooler thermal conditions.

The data presented in both **Chapter Five** and **Chapter Six** indicates that voluntary reductions in exercise intensity are associated with improvements in heat exchange over time, presumably aiding body temperature regulation. Thus, it can be reasonably concluded that voluntary reductions in exercise intensity are thermoregulatory behaviors. This suggests that self-paced exercise in the heat is a valid model by which to evaluate human thermoregulatory behavior. Notably, this conclusion is limited such that this exercise heat stress model has not been formally validated against another accepted human thermal behavioral experimental model. Examples of other experimental models include, but are certainly not limited to, the shuttle box model (Schlader et al. 2009) and the preferred ambient (Taylor et al. 1995) or skin (Cabanac et al. 1972; Flouris and Cheung 2008; Golja and Mekjavic 2003; Yogev et al. 2010; Yogev and Mekjavic 2009) temperature models. However, as there is not a ‘gold standard’ technique for evaluating human thermoregulatory behavior, a true validation may be impossible. Therefore, the conclusion that self-selected reductions in exercise intensity in the heat are thermoregulatory behaviors, as established via the definition of thermal behavior, appears justified.

10.2: General Aim II

Chapter Seven, **Chapter Eight** and **Chapter Nine**, attempted to elucidate the control of the thermoregulatory behavior identified within General Aim I. In a similar manner to that presented in Figure 2.24, these studies systematically tested the hypotheses proposed to mediate voluntary reductions in exercise intensity in the heat. This began with the direct role of \bar{T}_{sk} as a controller of exercise intensity (**Chapter Seven**) and subsequently,

thermal perception (**Chapter Eight**) and reductions in $\dot{V}O_{2\text{peak}}$ (**Chapter Nine**). The role of RPE in the voluntary selection of exercise intensity was also evaluated within these studies. However, this assessment was simply observational, and therefore rather indirect.

By utilizing an experimental methodology in which \bar{T}_{Sk} was either cooled or warmed during self-paced exercise, **Chapter Seven** demonstrated that \bar{T}_{Sk} plays an important role in the voluntary selection of exercise intensity upon exercise commencement. Interestingly, after the initial stages of exercise, \bar{T}_{Sk} appeared to play a less vital role. Additionally, RPE rose similarly irrespective of differences in exercise intensity, \bar{T}_{Sk} , or thermal perception, indicating that RPE was defended. Thus, \bar{T}_{Sk} has been formally identified as a controller of thermal behavior during exercise. However, from this study it remained unclear as to whether \bar{T}_{Sk} exerted its effects directly or indirectly via its influence on thermal perception and/or $\dot{V}O_{2\text{peak}}$.

In accordance, **Chapter Eight** attempted to elucidate the independent roles of (facial) skin temperature and thermal perception, i.e. thermal discomfort and sensation, in the voluntary, thermal, control of exercise intensity. In this paradigm the face, an area of high thermal sensitivity (e.g. Cotter and Taylor 2005; Nakamura et al. 2008), was thermally and non-thermally cooled, heated, or left alone while, under significant exogenous heat stress, exercise intensity was voluntarily selected in order to maintain a constant RPE. Thus, this novel experimental design permitted independent evaluation of (facial) skin temperature and thermal perception as controllers of exercise intensity, and therefore, thermoregulatory behavior. The results from this study demonstrated that both temperature and thermal perception are capable controllers of exercise intensity. Therefore, a change in temperature alone does not dictate these responses. Rather, thermal sensation and, ultimately, thermal discomfort are capable thermal behavioral controllers. It is also important to note that the data presented in **Chapter Eight** established a causal relationship between temperature regulation and the behavioral

modulation of exercise intensity, improving upon the associative nature of the conclusions made within General Aim I.

As dictated by elevations in \bar{T}_{sk} , the role of reductions in $\dot{V}O_{2peak}$, and the corresponding increase in the $\% \dot{V}O_{2peak}$ elicited by a given exercise intensity, were subsequently evaluated in **Chapter Nine**. Specifically, this study described the cardio-respiratory responses to self-paced exercise in the heat and evaluated these responses relative to those observed during peak exercise in the same environment. Accordingly, it was observed that any given submaximal exercise intensity elicited a higher $\% \dot{V}O_{2peak}$ in the heat. Interestingly, this observation was not associated with reductions in $\dot{V}O_{2peak}$, but rather, voluntary reductions in exercise intensity in the heat appeared related to an increased $\dot{V}O_2$ at a given submaximal exercise intensity. Thus, $\% \dot{V}O_{2peak}$ may play a role in the selection of exercise intensity, but not necessarily reductions in $\dot{V}O_{2peak}$, suggesting that sustainable exercise intensity is not always related to reductions in $\dot{V}O_{2peak}$. Furthermore, the RPE response in this study rose similarly irrespective of ambient temperature.

The data presented within the cohort of studies comprising General Aim II, represent a systematic evaluation of the controllers of thermal behavior during self-paced exercise in the heat. Accordingly, many of the hypotheses placed forth to explain reductions in exercise intensity in the heat have been tested (*see* Figure 2.24). The top portion of Figure 10.1 (in grey) represents a revised schematic by which exercise intensity is reduced in the heat as mediated by elevations in \bar{T}_{sk} and ultimately RPE, the controlling variable. Notably, it currently remains uncertain as to whether \bar{T}_{sk} only exerts its influence via its effects on thermal discomfort and/or $\% \dot{V}O_{2peak}$.

10.3: Limitations

Although shortcomings unique to each study are noted within each experimental chapter, the perspective from which this thesis has been written and the subsequent conclusions

drawn certainly have their limitations. In accordance, it is necessary to acknowledge the overall shortcomings of the data and the interpretation there of.

As mentioned in the introduction, the viewpoint from which this thesis has been written and the subsequent discussion of the data has been presented from a physiological perspective. That is, the role of behavior in temperature regulation has been emphasized, rather than the role of temperature regulation within behavior on the whole. Given this perspective the psychology of the control of human thermoregulatory behavior has likely been overlooked and therefore under discussed. Thus, it is likely that the interpretation of this data from a psychological perspective would contribute additional insights into the control of this behavior. Specifically, the role of temperature and thermoregulation on motivation, a psychological construct, would appear advantageous to investigate. Likewise, addressing the question of whether this behavior is mediated consciously and/or subconsciously would most certainly benefit from a psychological perspective.

Furthermore, care should be taken when interpreting the data presented in **Chapter Five**, **Chapter Six**, and **Chapter Seven**, as these data only provide associations between reductions in exercise intensity and changes in heat exchange (**Chapter Five and Chapter Six**) or \bar{T}_{sk} (**Chapter Seven**), rather than causation. For instance, in these chapters the role of temperature regulation in the control of exercise intensity in these studies cannot be differentiated from homeostatic regulation more globally. From a thesis-wide perspective however, the data presented in **Chapter Eight** certainly indicates a distinct, causal, role for temperature regulation as a modulator of exercise intensity. Nevertheless, as stand alone chapters these data should be interpreted as associative rather than causative.

Although it can certainly be argued that the findings presented in this thesis are not necessarily definitive, given the systematic nature in which these studies were conducted, the factors dictating the voluntary control of exercise intensity in the heat have certainly been made clearer. Perhaps most importantly however, our understanding of the control

of human thermoregulatory behavior on the whole has undoubtedly improved. Thus, despite these significant limitations, the overall purpose of this thesis was accomplished.

10.4: Considerations

Prior to discernable differences in T_C , reductions in exercise intensity in the heat appear to be primarily elicited by factors derived from elevations in \bar{T}_{Sk} (Abbiss et al. 2010; Ely et al. 2010; Tattersson et al. 2000; Tucker et al. 2004) (**Chapter Five, Chapter Six, Chapter Seven**). This arrangement is remarkably similar to that of the control of thermoregulatory behavior during rest, where heat balance is seemingly maintained via changes in \bar{T}_{Sk} (Cabanac et al. 1971; Schlader et al. 2009), and perhaps other intimately related factors. Given these apparent similarities, the ultimate focus of this thesis was not simply to understand the manner in which exercise intensity is controlled in the heat, but rather to elucidate the control of human thermoregulatory behavior more generally. Notably, as the self-paced exercise and exogenous heat stress model applies to situations in which T_C is controlled independent of differences in \bar{T}_{Sk} , the knowledge gained from this model appears to only be transferable to those situations in which behavior is primarily initiated by changes in \bar{T}_{Sk} . Importantly, this behavioral situation is perhaps that occurring most commonly.

In accordance, Figure 10.1 presents an overview of the control of human thermoregulatory behavior during both rest and exercise as initiated by \bar{T}_{Sk} . Notably, in this paradigm the cascade of physiological and perceptual responses elicited by \bar{T}_{Sk} similarly impacts the control of human thermoregulatory behavior during instances of both rest and exercise. The primary difference in the control of this behavior lies within that of the perceptual controller. At rest, thermal discomfort represents the controlling variable. However, during exercise, RPE is the controlling variable with thermal discomfort taking a more modulatory role. Another contrasting feature is that during rest behavior tends to correct deviations in \bar{T}_{Sk} , while during exercise, behavior alters metabolic heat production, and thus directly affects T_C . As can be observed (Figure 10.1), the control of thermal behavior during both rest and exercise is multi-factorial.

However, quite simply, during rest and exercise any factor directly altering thermal discomfort and/or RPE will modify behavior.

Control of Human Thermoregulatory Behavior during Rest and Exercise

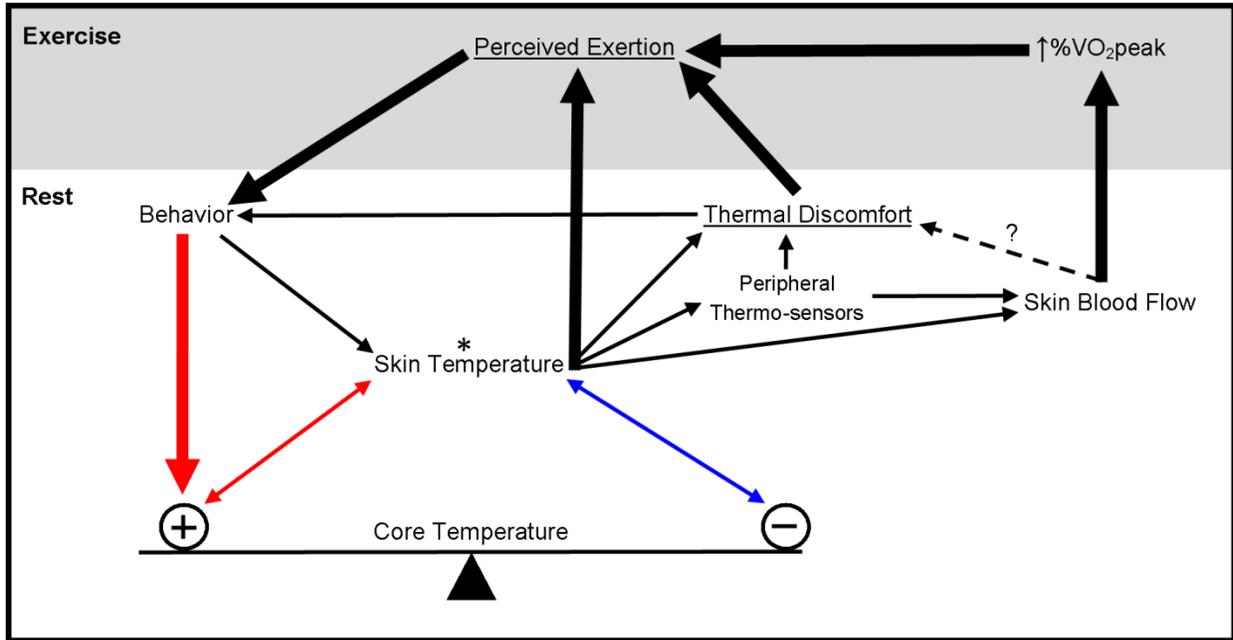


Figure 10.1: An integrative overview of the control of human thermoregulatory behavior during both rest and exercise in the heat as initiated (denoted by: *) by skin temperature (\bar{T}_{sk}). Rest (on bottom, in white) represents a state in which heat balance is behaviorally maintained (i.e. no change in T_C ; heat gain (+) = heat loss (-)), while during exercise (on top, in grey), the rise in T_C is behaviorally controlled independent of elevations in \bar{T}_{sk} . During both instances, \bar{T}_{sk} either directly or indirectly, via the activation of peripheral thermo-sensors and/or increases in skin blood flow, increases thermal discomfort. During rest, the appropriate behavior is initiated accordingly, as thermal discomfort is the controlling variable (denoted by: underline). By contrast, during self-paced exercise in the heat perceived exertion (RPE) is the controlling variable (denoted by: underline). In such instances, elevated \bar{T}_{sk} s either directly or via some combination of its effects on thermal discomfort, increases in skin blood flow and an increased percentage of peak oxygen uptake elicited by a given exercise intensity ($\% \dot{V}O_{2peak}$), increase RPE at a given intensity. As the rise in RPE is a protected perceptual variable during self-paced exercise, exercise intensity must therefore be reduced. This behavior reduces metabolic heat production and therefore heat gain, controlling the rise in T_C . Currently unknown

pathways are denoted by a ? and a dashed line. Pathways exclusive to exercise are denoted by bold arrows. All other arrows represent those pathways specific to a resting state or shared pathways. Pathways directly mediating heat gain and heat loss are denoted by red and blue lines. Note: Although not implicitly stated in text, prior to elevations in T_C , (local) skin temperature likely exerts its effects on skin blood flow both directly and via activation of peripheral thermo-sensors, which are likely dictated by different mechanisms (Johnson and Kellogg 2010).

10.5: Future Directions

With success, General Aim I attempted to establish self-paced exercise and heat stress as a thermal behavioral model. This conclusion is based on the established definition of thermal behavior and not on a validation against established thermal behavioral models. As discussed previously in this chapter (*see* 10.1: General Aim I), there are inherent difficulties in validating thermal behavioral models. Nevertheless, future studies are warranted in order to refine the exercise and heat stress model as a paradigm to further elucidate the control of human thermoregulatory behavior. For example, the fixed-RPE and heat stress protocol used in **Chapter Eight** is a seemingly valuable tool as it removes exercise performance as a potential motivation competing with thermal behavior. However, the repeatability of this protocol, and the effects of, for instance, heat acclimation and aerobic fitness level on this behavior are currently unknown.

Additionally, the thermal and non-thermal heating and cooling utilized in **Chapter Eight**, has introduced a unique experimental approach, which certainly lends itself to future research. For instance, in order to more definitively establish the independent nature of temperature and thermal perception, this experimental paradigm should be applied to other thermal behavioral models, e.g. voluntary exercise in the cold (Caputa and Cabanac 1980) or observing preferred skin temperature at rest (Cabanac et al. 1972; Flouris and Cheung 2008; Golja and Mekjavic 2003; Yogev et al. 2010; Yogev and Mekjavic 2009). Furthermore, as the physical changes in skin temperature in **Chapter Eight** were accompanied by changes in thermal perception, a logical ‘next step’ in evaluating the control of thermal behavior would be to evaluate the effects of changes in skin

temperature without changing thermal perception. Although changes in thermal perception are probably a pre-requisite initiating of thermal behavior, to date, this hypothesis remains untested.

Additional avenues for future research can be derived via both **Chapter Eight** and **Chapter Nine**. For instance, the factors identified within these chapters (i.e. an increased $\% \dot{V}O_{2\text{peak}}$ at a given exercise intensity and thermal perception) are likely not autonomous. Rather, they are probably complementary. For instance, given that $\dot{V}O_{2\text{peak}}$ is minimally affected when only \bar{T}_{sk} s are elevated (e.g. Arngrimsson et al. 2004), it is likely that thermal perception plays a large role in reducing exercise intensity during the initial stages of exercise. However, when T_C becomes substantially elevated and the deterioration of $\dot{V}O_{2\text{peak}}$ becomes more pronounced (e.g. Arngrimsson et al. 2004), reductions in $\dot{V}O_{2\text{peak}}$, and the accompanying increase $\% \dot{V}O_{2\text{peak}}$ at a given exercise intensity, likely play a larger role. Thus, in **Chapter Nine** the relatively small increase ($\sim +8\%$) in $\dot{V}O_2$ elicited by a given exercise intensity in the heat is probably not the sole explanation for the rather large reduction in exercise intensity ($\sim -22\%$). Thus, as observed in **Chapter Eight**, during the initial stages of exercise it is likely that thermal perception played a larger role. Notably, this hypothesis has yet to be experimentally tested.

In continuance, the manner in which T_C mediates reductions in exercise intensity in the heat would also be an area deserving investigation. For instance, it can be speculated that should T_C become elevated, T_C likely dictates the RPE response (Nielsen and Nybo 2003; Nybo and Nielsen 2001c; Rasmussen et al. 2004). This response is probably associated with (or driven by) a number of factors, including alterations in cerebral activity (Nielsen et al. 2001; Nybo and Nielsen 2001c; Rasmussen et al. 2004), reductions in voluntary neuromuscular activation (Morrison et al. 2004; Morrison et al. 2006; Morrison et al. 2009; Thomas et al. 2006), increased thermal discomfort (Attia and Engel 1981, 1982; Cabanac et al. 1972; Cabanac et al. 1971; Chatonnet and Cabanac 1965; Mower 1976), and reductions in $\dot{V}O_{2\text{peak}}$ (Arngrimsson et al. 2004; Arngrimsson et al. 2003; Dimri et

al. 1980; Nybo et al. 2001; Sawka et al. 1985; Wingo et al. 2005). At present however, the contribution of these responses to the decision to reduce exercise intensity in the heat remains uncertain. It is noteworthy however, that the contribution of a given factor will likely vary with the magnitude of hyperthermia.

Finally, skin blood flow responses appear to be an important and intriguing, yet overlooked, component potentially affecting human thermoregulatory behavior. During exercise, increases in skin blood flow are likely ultimately responsible for the reductions in $\dot{V}O_{2peak}$, and subsequent increases in $\% \dot{V}O_{2peak}$. However, this hypothesis has yet to be successfully tested as altering whole-body skin blood flow without changing thermal perception, a potentially confounding factor, has yet to be achieved. During rest, the role of skin blood flow in thermoregulatory behavior remains even more uncertain. Nevertheless, of particular importance may be that of locally modulated skin blood flow, which is controlled independent of changes in T_c (Bregelmann and Savage 1997; Savage and Bregelmann 1996). In this paradigm, any factor that alters the local control of skin blood flow may, in turn, affect thermal discomfort and therefore, thermal behavior. However, at present this remains a virtually untested hypothesis. Nevertheless, the initial efforts within this research area should attempt to identify the relative activity of local and/or reflex controlled skin blood flow during instances where there is freedom to thermally behave.

10.6: Conclusions

The purpose of this thesis was to elucidate some of the mechanisms by which temperature regulation dictates human behavior during exercise. This specifically entailed identifying voluntary reductions in intensity during self-paced exercise as thermoregulatory behaviors and then evaluating the manner in which this specific behavior is controlled. In accordance, from the studies presented in this thesis designed to test the hypotheses presented in **Chapter Three** it can be concluded that:

- 1.) During self-paced exercise in uncompensable heat, voluntary reductions in exercise intensity improve heat exchange between the body and the environment, and thus, improve the capability to regulate body temperature.
- 2.) Self-selected reductions in exercise intensity during exercise in the heat are, by definition, thermoregulatory behaviors. Therefore, self-paced exercise with exogenous heat stress appears to be a valid experimental model by which to evaluate the control of human thermoregulatory behavior.
- 3.) During the initial stages of exercise \bar{T}_{Sk} is inversely related to exercise intensity. Therefore, \bar{T}_{Sk} is a capable thermal controller of self-selected exercise intensity, and thus, thermal behavior during exercise.
- 4.) A change in (local) skin temperature is not a requirement for the initiation of thermoregulatory behavior in humans. Rather, peripherally mediated thermal sensation and thermal discomfort are capable modulators of exercise intensity in the heat.
- 5.) When only \bar{T}_{Sk} is elevated, voluntary reductions in exercise intensity are associated with an increased $\% \dot{V}O_{2peak}$ elicited by a given exercise intensity. However, this is not mediated by reductions in $\dot{V}O_{2peak}$, but rather, an increase in $\dot{V}O_2$ at a given exercise intensity.
- 6.) The RPE response during self-paced exercise is maintained independent of ambient or \bar{T}_{Sk} , and is dictated predominantly by the relative proportion of the exercise task completed. Thus, RPE represents the controlling variable during self-paced exercise in the heat.

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APPENDIX A

A: Ethical Approval Documentation

Chapter Five



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18 November 2009

Mr Zachary Schlader
IFNHH
PN452

Dear Zac

**Re: HEC: Southern A Application – 09/62
Fixed-intensity versus self-paced exercise in the heat**

Thank you for your letter dated 17 November 2009.

On behalf of the Massey University Human Ethics Committee: Southern A, I am pleased to advise you that the ethics of your application are now approved. Approval is for three years. If this project has not been completed within three years from the date of this letter, reapproval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

Yours sincerely



Professor Julie Boddy, Chair
Massey University Human Ethics Committee: Southern A

cc Dr Toby Mundel	Dr Steve Stannard	Prof Richard Archer
IFNHH	IFNHH	IFNHH
PN452	PN452	PN452

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Te Kōwhiri
Ki Pūrehoro

Chapter Six and Chapter Nine


MASSEY UNIVERSITY

5 August 2010

Mr Zachary Schlader
IFNHH
PN452

Dear Zachary

Re: HEC: Southern A Application – 10/38
The effects of 40°C heat stress on the conscious selection of exercise work-rate

Thank you for your letter dated 5 August 2010.

On behalf of the Massey University Human Ethics Committee: Southern A, I am pleased to advise you that the ethics of your application are now approved. Approval is for three years. If this project has not been completed within three years from the date of this letter, reapproval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

Yours sincerely



Professor Julie Boddy, Chair
Massey University Human Ethics Committee: Southern A

cc Dr Toby Mundel IFNHH PN452	Dr Stephen Stannard IFNHH PN452	Prof Richard Archer, HoI IFNHH PN452
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Chapter Seven



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5 August 2009

Mr Zachary Schlader
IFNHH
PN452

Dear Zac

**Re: HEC: Southern A Application – 09/44
The effect of skin temperature on exercise performance**

Thank you for your letter dated 30 July 2009.

On behalf of the Massey University Human Ethics Committee: Southern A, I am pleased to advise you that the ethics of your application are now approved. Approval is for three years. If this project has not been completed within three years from the date of this letter, reapproval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

Yours sincerely



Professor Julie Boddy, Chair
Massey University Human Ethics Committee: Southern A

cc Dr Toby Mundel IFNHH PN452	Dr Stephen Stannard IFNHH PN452	Prof Richard Archer, Hol IFNHH PN452
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Massey University Human Ethics Committee
Accredited by the Health Research Council

Te Kaitiaki
Ki Pūrehuroa

Chapter Eight



MASSEY UNIVERSITY

3 March 2010

Mr Zac Schlader
IFNHH
PN452

Dear Zac

Re: HEC: Southern A Application – 10/05
The role of temperature and perception in the control of exercise intensity

Thank you for your letter dated 2 March 2010.

On behalf of the Massey University Human Ethics Committee: Southern A, I am pleased to advise you that the ethics of your application are now approved. Approval is for three years. If this project has not been completed within three years from the date of this letter, reapproval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

Yours sincerely



Professor Julie Boddy, Chair
Massey University Human Ethics Committee: Southern A

cc Prof Richard Archer, Hol
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APPENDIX B

B: Statements of Contribution

Chapter Two

DRC 16



MASSEY UNIVERSITY
GRADUATE RESEARCH SCHOOL

**STATEMENT OF CONTRIBUTION
TO DOCTORAL THESIS CONTAINING PUBLICATIONS**

(To appear at the end of each thesis chapter/section/appendix submitted as an article/paper or collected as an appendix at the end of the thesis)

We, the candidate and the candidate's Principal Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of Candidate: Zachary J. Schlader.....

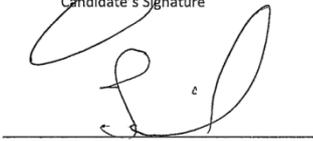
Name/Title of Principal Supervisor: Dr. Toby Mundel.....

Name of Published Paper: Human thermoregulatory behavior during rest and exercise - A prospective review.....

.....

In which Chapter is the Published Work: Chapter 2.....

What percentage of the Published Work was contributed by the candidate: 85%.....

 _____ Candidate's Signature	<u>02/05/2011</u> Date
 _____ Principal Supervisor's signature	<u>2/5/2011</u> Date

GRS Version 2-1 December 2010

Chapter Five

DRC 16


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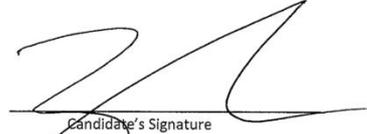
Name of Candidate: Zachary J. Schlader

Name/Title of Principal Supervisor: Dr. Toby Mundel

Name of Published Paper: Exercise and heat stress: Performance, fatigue and exhaustion

In which Chapter is the Published Work: Chapter 5

What percentage of the Published Work was contributed by the candidate: 85%


Candidate's Signature

02/05/2011
Date


Principal Supervisor's signature

2/5/2011
Date

GRS Version 2- 1 December 2010

Chapter Five

DRC 16



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We, the candidate and the candidate's Principal Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of Candidate: Zachary J. Schlader

Name/Title of Principal Supervisor: Dr. Toby Mundel

Name of Published Paper: Exercise modality modulates body temperature regulation during exercise under uncompensable heat stress

In which Chapter is the Published Work: Chapter 5

What percentage of the Published Work was contributed by the candidate: 85%


Candidate's Signature

02/05/2011
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Principal Supervisor's signature

2/5/2011
Date

Chapter Six

DRC 16



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Name of Candidate: Zachary J. Schlader

Name/Title of Principal Supervisor: Dr. Toby Mundel

Name of Published Paper: Evidence for thermoregulatory behavior during self-paced exercise in the heat

In which Chapter is the Published Work: Chapter 6

What percentage of the Published Work was contributed by the candidate: 85%


Candidate's Signature

09/09/2011
Date


Principal Supervisor's signature

09/09/2011
Date

Chapter Seven

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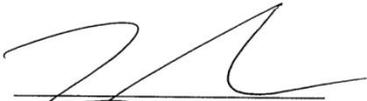
Name/Title of Principal Supervisor: Dr. Toby Mundel.....

Name of Published Paper: Skin temperature as a thermal controller of exercise intensity.....

.....

In which Chapter is the Published Work: Chapter 7.....

What percentage of the Published Work was contributed by the candidate: 85%.....


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2/5/2011
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Chapter Eight

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Name of Candidate: Zachary J. Schlader.....

Name/Title of Principal Supervisor: Dr. Toby Mundel.....

Name of Published Paper: The independent roles of temperature and thermal perception in the control of
human thermoregulatory behavior.....

In which Chapter is the Published Work: Chapter 8.....

What percentage of the Published Work was contributed by the candidate: 85%.....

Candidate's Signature

02/05/2011
Date

Principal Supervisor's signature

2/5/2011
Date

Chapter Nine

DRC 16



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STATEMENT OF CONTRIBUTION
TO DOCTORAL THESIS CONTAINING PUBLICATIONS

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We, the candidate and the candidate's Principal Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of Candidate: ...Zachary J. Schlader.....

Name/Title of Principal Supervisor: ...Dr. Toby Mundel.....

Name of Published Paper: ...Is peak oxygen uptake a determinant of moderate duration self-paced exercise
performance in the heat?.....

In which Chapter is the Published Work: ...Chapter 9.....

What percentage of the Published Work was contributed by the candidate: ...85%.....


Candidate's Signature

09/09/2011
Date


Principal Supervisor's signature

09/09/2011
Date

APPENDIX C

C: Published Papers

Chapter Two

Physiology & Behavior 99 (2010) 269–275



Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb



Review

Human thermoregulatory behavior during rest and exercise – A prospective review

Zachary J. Schlader*, Stephen R. Stannard, Toby Mündel

Exercise and Sport Science, Massey University, Private Bag 11 222, Palmerston North, 4442, New Zealand

ARTICLE INFO

Article history:
 Received 8 September 2009
 Received in revised form 8 November 2009
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Keywords:
 Thermo-behavior
 Thermal comfort
 Thermal sensation
 Perceived exertion
 Skin temperature

ABSTRACT

Despite the important role of temperature regulation in human behavior, it is frequently overlooked as a thermoregulatory response during both rest and exercise. During rest, the initiation of thermoregulatory behavior is preceded by changes in thermal comfort/sensation, with the temperature of the skin playing a vital signaling role. This behavior maintains heat balance and prevents the activation of autonomic thermoregulatory responses. Recently, self-paced exercise in the heat has been used as a thermo-behavioral model and accordingly, reductions in exercise work-rate in the heat appear sufficient to maintain regulation. Similar to rest, this behavior is mediated by elevations in skin temperature, however the perception of effort appears to be the perceptual trigger.

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1. Introduction

Thermoregulatory behavior (thermo-behavior) is a coordinated action establishing an optimal condition for heat exchange between the environment and the body, and depending on the circumstance this could include situations entailing heat loss, heat gain, or heat balance [1]. While typically viewed as a primitive thermoregulatory response [i.e. poikilothermic; e.g. 2,3], all animals employ this powerful thermoregulatory means. Humans provide an interesting model for the study of thermo-behavior; not only do we have thermoregulatory capabilities beyond that of behavior, but we can also contribute subjective feedback helping to unlock the mechanisms underlying this behavior.

By definition, temperature regulation refers to the maintenance of body temperatures within a narrow range [1], and in humans the regulated temperature is that of the body core, which is physiologically defended by both autonomic and behavioral responses. The autonomic responses have a relatively limited capacity, while thermo-behavioral capabilities are virtually unlimited, exceeding those of changes, for example, in metabolism [4] or sweating. Accordingly, although frequently overlooked as a physiological variable, behavioral temperature regulation is a crucial thermoregulatory means during both rest and exercise.

At rest the suggested role of thermo-behavior is avoidance of an impending thermal insult, acting to maintain heat balance and

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 doi:10.1016/j.physbeh.2009.12.003

Chapter Five

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Editorial

Exercise and heat stress: performance, fatigue and exhaustion—a hot topic

Z J Schlader, S R Stannard, T Mündel

Fatigue is suggested to be a general concept that is characterised by an acute impairment in performance and leads to the eventual inability to produce the necessary force, that is, volitional exhaustion.¹ Homeostasis is maintained by the physiological regulatory processes occurring throughout the body,² and during exercise, the development of fatigue and exhaustion is proposed to prevent homeostatic failure.³ Principle to the regulatory systems maintaining homeostasis is that of thermoregulation, and as such the combined stressors of exercise and heat stress are used as a model to investigate the regulatory processes that influence physical performance, the development of fatigue and the onset of exhaustion.⁴⁻⁵ Accordingly, theories have been developed, healthy (lively) debate has arisen and various journals have seen fit to devote special issues—for example, *Sports Medicine* (vol 37, issues 4–5), *Journal of Applied Physiology* (vol 104, issue 5) and timely reviews.⁴⁻⁷

Within the exercise and heat stress model, two exercise protocols have been used that both describe performance as a dependent variable of time: (1) fixed-intensity (ie, constant workload) exercise—exercise is undergone until volitional exhaustion, and (2) self-paced exercise—which evaluates the time to complete a given task (eg, a set amount of work) where the workload can be adjusted by the exerciser. Both exercise time-to-exhaustion and self-paced exercise performance have been found to be attenuated under heat stress.⁸⁻¹⁶ However, confounding these conclusions is that these exercise protocols evaluate a different combination of physiological processes. Fixed-intensity exercise provides a measure of exhaustion, whereas self-paced exercise provides an indication

of the development of fatigue; and arising from this limitation, seemingly opposing theories have developed.

Thermoregulation is attained by both passive (ie, non-regulated) and active (ie, regulated) systems.¹⁷ During exercise in the heat, passive heat loss (eg, evaporation, conduction) is maximised by the regulation of active thermoregulatory mechanisms (ie, autonomic and/or behavioural). When the heat loss required for heat balance is exceeded by metabolic heat production (ie, uncompensable heat stress), thermoregulation is dependent on behavioural adjustments in metabolic heat production, which is proportional to exercise work rate.¹⁸

During fixed-intensity exercise in the heat, metabolic heat production is constant, heat loss is limited solely to autonomic mechanisms and thus a proportional, passive (ie, non-regulated) rise in core temperature ensues. Under these conditions, thermoregulation mediates voluntary (ie, behavioural) exercise exhaustion upon the attainment of a core temperature of approximately 40°C,^{8 10 13 14} although the absolute temperature at which exhaustion occurs varies with aerobic fitness.⁹ These findings contribute to the theory that exercise duration in the heat is limited by a *critical core temperature*^{6 19} with this threshold core temperature presumably preventing the development of exertional heat stroke, which, in combination with other signs and symptoms, is characterised by a core temperature >40°C.²⁰ It is acknowledged, however, that this *critical core temperature* of approximately 40°C is primarily a laboratory-based phenomenon because this core temperature threshold can be exceeded during “real-world” situations. For instance, during competitive situations, core temperatures in highly trained runners have been found to exceed 40°C without any indication of the development of heat illness,^{21 22} suggesting that thermoregulation was not compromised by a high core temperature in these athletes.

In contrast, during self-paced exercise the thermal compensability of the

environment can be manipulated by the exerciser through adjustments in work rate (ie, metabolic heat production). These behavioural adjustments in work rate result in a regulated rise in core temperature and permit completion of the exercise task while avoiding the attainment of a critically high core temperature. However, the consequence of this behaviour is a reduction in exercise performance,^{11 12 15 16} which provides the theoretical basis for the theory of *anticipatory regulation and avoidance*.⁷

Given that fixed-intensity and self-paced exercise protocols evaluate different physiological phenomena (eg, exhaustion and fatigue, respectively), the theories of the *critical core temperature* and *anticipatory regulation and avoidance* have been built up as mutually exclusive⁶ and alternatives of each other.¹⁹ However, it has recently been suggested that these theories actually complement one another and are in fact “safety” mechanisms⁶ acting to maintain thermoregulation. Yet, despite the suggestion that future research should try to incorporate both fixed-intensity and self-paced exercise protocols,⁶ an established relationship between *anticipatory regulation* and a *critical core temperature* has remained elusive, suggesting that these theories are conflicting.

It is proposed here that *anticipatory regulation* and *critical core temperature* exist on a continuum. At one end of this continuum is voluntary exhaustion, which occurs immediately before loss of thermoregulation, although fatigue is the progression of processes that potentially develop into this exhaustion. To test this proposal we conducted a retrospective analysis of the physiological strain at exhaustion or completion of both fixed-intensity and self-paced exercise protocols, respectively. Physiological strain was indicated by the physiological strain index (PSI), modified from Moran *et al.*²³ The PSI was chosen for this analysis because it mathematically accounted for the limitation posed by elevations in body temperature.

Mean heart rates and core temperatures before exercise and at exhaustion (fixed-intensity exercise) or completion (self-paced exercise) were used as noted in the published manuscripts. Despite there being a relatively large selection of literature, the studies used for this analysis were chosen based on the availability of published mean data. If the necessary data at the conclusion of the exercise bouts were unavailable, the study was excluded. Hence, this resulted in the inclusion of four (of the seven considered) for

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Br J Sports Med January 2011 Vol 45 No 1

3

Chapter Five

Eur J Appl Physiol
DOI 10.1007/s00421-010-1692-3

ORIGINAL ARTICLE

Exercise modality modulates body temperature regulation during exercise in uncompensable heat stress

Zachary J. Schlader · Aaron Raman ·
R. Hugh Morton · Stephen R. Stannard ·
Toby Mündel

Accepted: 5 October 2010
© Springer-Verlag 2010

Abstract This study evaluated exercise modality [i.e. self-paced (SP) or fixed-intensity (FI) exercise] as a modulator of body temperature regulation under uncompensable heat stress. Eight well-trained male cyclists completed (work-matched) FI and SP cycling exercise bouts in a hot ($40.6 \pm 0.2^\circ\text{C}$) and dry (relative humidity $23 \pm 3\%$) environment estimated to elicit 70% of $\dot{V}\text{O}_2\text{max}$. Exercise intensity (i.e. power output) decreased over time in SP, which resulted in longer exercise duration (FI 20.3 ± 3.4 min, SP 23.2 ± 4.1 min). According to the heat strain index, the modification of exercise intensity in SP improved the compensability of the thermal environment which, relative to FI, was likely a result of the reductions in metabolic heat production (i.e. $\dot{V}\text{O}_2$). Consequently, the rate of rise in core body temperature was higher in FI ($0.108 \pm 0.020^\circ\text{C}/\text{min}$) than in SP ($0.082 \pm 0.016^\circ\text{C}/\text{min}$). Interestingly, cardiac output, stroke volume, and heart rate during exercise were independent of exercise modality. However, core body temperature (FI $39.4 \pm 0.3^\circ\text{C}$, SP $39.1 \pm 0.4^\circ\text{C}$), blood lactate (FI 2.9 ± 0.8 mmol/L, SP 2.3 ± 0.7 mmol/L), perceived exertion (FI 18 ± 2 , SP 16 ± 2), and physiological strain (FI 9.1 ± 0.9 , SP 8.3 ± 1.1) were all higher in FI compared to SP at exhaustion/completion. These findings indicate that, when exercise is SP, behavioral modification of metabolic heat production improves the compensability

of the thermal environment and reduces thermoregulatory strain. Therefore, under uncompensable heat stress, exercise modality modulates body temperature regulation.

Keywords Fixed-intensity exercise · Self-paced exercise · Thermoregulatory behavior · Thermal compensability · Metabolic heat production

Introduction

Body temperature is controlled by the regulation of autonomic and/or behavioral responses that modulate body heat exchange (Romanovsky 2007). According to the heat balance equation, when heat gain outweighs heat loss, body heat storage increases, elevating body temperatures. During fixed-intensity (FI) (constant power) exercise, metabolic heat production is constant, and therefore, heat loss is limited solely to autonomic responses. Consequently, core body temperature rises until heat balance is achieved as indicated by a 'plateau' in core temperature (Nielsen and Nielsen 1962; Saltin and Hermansen 1966).

During FI exercise when exposed to uncompensable heat stress, the attainment of heat balance is impossible (Cheung et al. 2000) with core temperature rising linearly as a function of the metabolic and ambient heat loads (Robinson 1963) until exhaustion occurs (Cheung 2007; Cheung and Sleivert 2004). This inability to continue exercising in a hot environment, i.e. heat exhaustion (Armstrong et al. 2007), is directly associated with the failure to achieve heat balance as heat exhaustion is accompanied by high core temperatures (Gonzalez-Alonso et al. 1999) and an increased challenge for the cardiovascular system to simultaneously meet the demands for both the working musculature and temperature regulation

Communicated by George Havenith.

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S. R. Stannard · T. Mündel
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Published online: 27 October 2010

 Springer

Chapter Six

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Journal of Thermal Biology ■ (■■■■) ■■■-■■■



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Evidence for thermoregulatory behavior during self-paced exercise in the heat

Zachary J. Schlader*, Stephen R. Stannard, Toby Mündel

School of Sport and Exercise, Massey University, Private Bag 11 222, Palmerston North 4442, New Zealand

ARTICLE INFO

Article history:
Received 18 April 2011
Accepted 6 July 2011

Keywords:
Thermal behavior
Exercise intensity
Thermal discomfort
Thermal compensability

ABSTRACT

The primary objective of this investigation was to test the hypothesis that voluntary reductions in exercise intensity in heat improve heat exchange between the body and the environment, and are thus thermoregulatory behaviors. This was accomplished by observing the conscious selection of exercise intensity and the accompanying thermal outcomes of eleven moderately active males when exposed to an uncompensably hot (UNCOMP) and a compensable (COMP) thermal environment. Evidence for thermoregulatory behavior was defined relative to the specific, pre-determined definition. Self-selected exercise intensity (power output) was unanimously reduced in UNCOMP over time and relative to COMP in all the subjects. These voluntary responses were found to modify metabolic heat production over time and therefore heat exchange between the body and the environment. Likewise, the observed reductions in power output were, at least in part, due to a conscious action, that was found to be inversely related to the total body heat storage and thermal discomfort. There was no evidence for thermoregulatory behavior in COMP. These data uniquely indicate that voluntary reductions in exercise intensity improves heat exchange over time, and therefore contributes to the regulation of body temperature. These findings suggest that reductions in exercise intensity in heat are, by definition, thermoregulatory behaviors.

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1. Introduction

Behavior is generally thought to be the most effective form of temperature regulation (Parsons, 2003) and compared to the relatively restricted capacity of the autonomic thermoregulatory responses, behavioral responses are nearly limitless (Benzinger, 1969). Thus, behavior is regarded as the 'first line of defense' in maintaining body temperature (Werner et al., 2008). However, difficulty in determining functional relationships between thermal stressors and the ensuing behavior means that relatively little is known about the control of human thermoregulatory behavior. Hence, the development of models to evaluate thermal behavior in humans is of importance.

A notable example of thermoregulatory behavior in humans is voluntary exercise (Mercer, 2001). This is observed most commonly when a person voluntarily increases heat production by exercising when cold (Caputa and Cabanac, 1980). Interestingly, the selected intensity of this exercise is inversely related to ambient temperature (Cabanac and Leblanc, 1983). Therefore, it is perhaps not surprising that exercise intensity is voluntarily reduced in heat (Budd, 2001; Ely et al., 2010; Tattersson et al., 2000; Tucker et al., 2004). Thus, self-paced exercise under environmental stress has been suggested to

provide meaningful information concerning the control of thermal behavior in humans (Flouris, 2010; Schlader et al., 2010). However, in order to assert self-paced exercise in heat as a model to evaluate human thermoregulatory behavior, a thorough investigation of the behavioral and thermal outcomes of the voluntary selection of exercise intensity in heat is warranted.

The primary objective of this investigation was to test the hypothesis that voluntary reductions in exercise intensity in heat modify heat exchange between the body and the environment, and are thus thermoregulatory behaviors. This was accomplished by observing the conscious selection of exercise intensity during exposure to an uncompensably hot (UNCOMP) and a compensable (COMP) thermal environment. Within this uncompensable heat stress paradigm, as the autonomic capability for heat exchange is maximized and autonomically induced heat balance is impossible (Cheung et al., 2000), it was assumed that any modification of heat exchange over time must be driven by alterations in exercise intensity (Schlader et al., 2011a).

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doi:10.1016/j.jtherbio.2011.07.002

2. Methods

2.1. Experimental overview

In UNCOMP and COMP, each of the eleven male volunteers completed self-paced exercise bouts on a cycle ergometer.

Please cite this article as: Schlader, Z.J., et al., Evidence for thermoregulatory behavior during self-paced exercise in the heat. *J. Thermal Biol.* (2011), doi:10.1016/j.jtherbio.2011.07.002

Chapter Seven

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ORIGINAL ARTICLE

Skin temperature as a thermal controller of exercise intensity

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Abstract This study examined the role of skin temperature on self-selected exercise intensity (i.e., power output). Eight well-trained, male cyclists completed two 60 min self-paced cycling bouts during which they completed as much work as possible. Using a liquid-perfused suit, skin temperature (T_{sk}) was changed during the two trials such that T_{sk} either started hot and was cooled (H to C) or started cold and was heated (C to H) throughout exercise. Pre-exercise core temperatures (T_c) and heart rates (HR) were similar between trials, while T_{sk} , thermal comfort and thermal sensation were higher in H to C. The change in T_{sk} was similar in magnitude during the two trials. Work completed was greatest in C to H, which was attributed to a higher initial power output. T_c was similar between trials. HR was similar until 35 min had elapsed, after which it became lower in H to C. The perception of effort increased similarly between the two trials, while thermal comfort and thermal sensation generally reflected the changes observed in T_{sk} . These results indicate that upon exercise commencement T_{sk} and the accompanying thermal perceptions are important inputs in the initial selection of exercise intensity.

Keywords Temperature regulation · Exercise intensity · Metabolic heat production · Thermoregulatory behavior

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Introduction

Behavior is generally considered to be the most effective (Parsons 2003) and limitless (Benzinger 1969) form of temperature regulation. Classic examples include, but are not limited to, adding or removing clothing, changing body positions, and adjusting the thermostat in a room. Notably, voluntary exercise is also a mode of thermoregulatory behavior (Mercer 2001), with voluntary muscular work in a cold environment resulting in the attainment of thermal comfort (Caputa and Cabanac 1980). However, rarely during exercise is producing enough heat a problem; more often it is the dissipation of this metabolic heat that challenges (temperature) regulation. Accordingly, self-paced exercise in the heat has been suggested as a model to evaluate thermoregulatory behavior (Morante and Brotherhood 2008; Schlader et al. 2010c). This model states that the compensability of the thermal environment can be manipulated by the exerciser through self-selected adjustments in the rate of metabolic heat production, i.e., exercise intensity (Schlader et al. 2010b). This behavior permits successful completion of the exercise task; however, as a consequence, exercise performance in the heat is reduced relative to more moderate thermal conditions (Marino et al. 2004; Marino et al. 2000; Tattersson et al. 2000; Tucker et al. 2004).

Behavioral reductions in exercise intensity in the heat do not appear to be associated with increased levels of cardiovascular, thermoregulatory, or metabolic strain (Marino 2004). For instance, compared to exercise in a more moderate thermal environment, exercise intensity in the heat has been found to be reduced prior to any significant differences in heart rate, core temperature, or indicators of metabolism (Tattersson et al. 2000; Tucker et al. 2004). Accordingly, the signaling input(s) for these responses is

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Chapter Eight

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The independent roles of temperature and thermal perception in the control of human thermoregulatory behavior

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ABSTRACT

The present study independently evaluated temperature and thermal perception as controllers of thermoregulatory behavior in humans. This was accomplished using a self-paced exercise and heat stress model in which twelve physically active male subjects exercised at a constant subjective rating of perceived exertion (16, hard – very hard) while their face was thermally and non-thermally cooled, heated, or left alone (control trial). Thermal cooling and heating were achieved via forced convection, while non-thermal cooling and heating were accomplished via the topical application of menthol and capsaicin solutions. Evidence for thermoregulatory behavior was defined in terms of self-selected exercise intensity, and thus exercise work output. The results indicate that, in the absence of changes in temperature, non-thermal cooling and warming elicited thermal sensory and discomfort sensations similar to those observed during thermal cooling and warming. Furthermore, the perception of effort was maintained throughout exercise in all trials, while the initial and final exercise intensities were also similar. Thermal and non-thermal cooling resulted in the highest work output, while thermal warming the lowest. Non-thermal warming and control trials were similar. Heart rate, mean skin and core (rectal) temperatures, and whole body and local (neck) sweat rates were similar between all trials. These data indicate that changes in temperature are not a requirement for the initiation of thermoregulatory behavior in humans. Rather, thermal sensation and thermal discomfort are capable behavioral controllers.

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1. Introduction

By definition, a thermoregulatory behavior establishes a preferred condition for heat exchange between an organism and its environment [1], thereby helping to ensure survival and optimize comfort [2]. Compared to the relatively restricted capacity of autonomic thermoregulatory responses, behavioral responses are considered to be nearly limitless [3] and are thus regarded as the ‘first line of defense’ in maintaining body temperatures [4].

Via their influence on thermal sensation [5] and thermal discomfort [6], both skin and core body temperatures are capable initiators of thermoregulatory behavior [7–14]. However, when given behavioral freedom, core temperature changes too slowly for it to be the primary thermal signal [15], indicating that skin temperature is most likely the preferred behavioral input [9,13]. This arrangement effectively prevents unnecessary activation of water and/or energy consuming autonomic thermoregulatory responses [16], while suitably defending core body temperature [17].

The voluntary control of exercise intensity (work output), and therefore metabolic heat production, when exposed to both cold and hot environments provides valuable insights into the control of human thermoregulatory behavior [17]. For example, in the cold, thermal discomfort is improved by increases in exercise intensity [18,19], while in the heat, voluntary reductions in work/exercise intensity effectively prevent body temperatures from rising excessively [20–22]. Thus, self-paced exercise under environmental stress provides meaningful information concerning the control of thermoregulatory behavior in humans [17,23].

Given the causal relationships between body temperatures and the perception thereof, the fundamental mechanisms controlling human thermoregulatory behavior remain uncertain. For instance, skin temperature, and the associated thermal perceptions, influences the voluntary selection of exercise intensity [14], but it is unclear as to whether a change in temperature must occur in order for this thermal behavior to be initiated. Indeed, it is highly possible that a change in thermal sensation, and thus discomfort, independent of changes in temperature is capable of commencing thermal behavioral responses.

Utilizing the aforementioned self-paced exercise model, the purpose of this study was to independently evaluate temperature and thermal perception as controllers of human thermoregulatory behavior. Under heat stress, subjects were instructed to exercise at a

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Chapter Nine

IS PEAK OXYGEN UPTAKE A DETERMINANT OF MODERATE DURATION SELF-PACED EXERCISE PERFORMANCE IN THE HEAT?

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APPENDIX E

E: Chapter Five Retrospective Analysis Methodology

E.1: Overview

As part of the pilot testing for **Chapter Five**, a retrospective analysis of the previously published literature was undergone. In this analysis the physiological strain at exhaustion/completion of both fixed-intensity (FI) and self-paced (SP) exercise in the heat were directly compared using the physiological strain index (PSI), modified from Moran et al. (1998). The PSI was chosen for this analysis as it mathematically accounted for the physiological limitations posed by elevations in body temperature.

E.2: Use of the Physiological Strain Index

Mean heart rates (HR) and core body temperatures (T_C) prior to exercise and at exhaustion (FI) or completion (SP) were used as noted in the published manuscripts. Despite there being a relatively large selection of literature, the studies used for this analysis were chosen based on the availability of published mean data. If the necessary data at the conclusion of the exercise bouts were unavailable the study was excluded. Hence, this resulted in the inclusion of four (of the seven considered) for FI and four (of four) for SP.

While data at the termination of exercise was not compromised, if pre-exercise HR or T_C were not provided 60 bpm and 37.0°C were used as estimates. In the original PSI maximal core temperature was ethically limited to 39.5°C, but given that T_C was allowed to approach, and in some cases exceed 40.0°C in the literature reviewed, the original PSI was modified to allow for a maximal T_C of 40.0°C.

Despite the relatively small number of studies used in the analysis, the PSI was regarded as an appropriate platform for comparing the level of physiological strain at the conclusion of FI and SP exercise. However, it is acknowledged that the PSI is a somewhat crude method of evaluating physiological strain, and that it does not take into account methodological differences concerning T_C measurement location, and exercise

mode or intensity. However, given the definition of the thermal core (“those inner tissues of the body whose temperatures are not changed in their relationship to each other by circulatory adjustments and changes in heat dissipation to the environment... (Mercer 2001)”), that all studies utilized one of the acceptable methods of measuring T_C (i.e. either esophageal or rectal temperature) (Mercer 2001), and that a maximal exercise effort was assumed in all instances, these limitations were considered acceptable. Further, given the precise regulation of core temperature, the subjects’ relatively high level of aerobic fitness, and that fluctuations in resting T_C and HR $\pm 1.0^\circ\text{C}$ and 10 bpm, did not significantly affect ($P>0.05$) the PSI outcome, 37.0°C and 60 bpm were deemed sufficient estimates where resting core temperature and heart rate data were unavailable.

E.3: Statistical Analysis

The effect of exercise modality on final HR, T_C , and PSI was determined via independent *t*-tests.